ORGANIC ARSENICAL COMPOUNDS

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GENERAL INTRODUCTION

American Chemical Society Series of Scientific and Technologic Monographs

By arrangement with the Interallied Conference of Pure and Applied Chemistry, which met in London and Brussels in July, 1919, the American Chemical Society was to undertake the production and publication of Scientific and Technologic Monographs on chemical subjects. At the same time it was agreed that the National Research Council, in coöperation with the American Chemical Society and the American Physical Society, should undertake the production and publication of Critical Tables of Chemical and Physical Constants. The American Chemical Society and the National Research Council mutually agreed to care for these two fields of chemical development. The American Chemical Society named as Trustees, to make the necessary arrangements for the publication of the monographs, Charles L. Parsons, Secretary of the American Chemical Society, Washington, D. C.; John E. Teeple, Treasurer of the American Chemical Society, New York City; and Professor Gellert Alleman of Swarthmore College. The Trustees have arranged for the publication of the American Chemical Society series of (a) Scientific and (b) Technologic Monographs by the Chemical Catalog Company of New York City.

The Council, acting through the Committee on National Policy of the American Chemical Society, appointed the editors, named at the close of this introduction, to have charge of securing authors, and of considering critically the manuscripts prepared. The editors of each series will endeavor to select topics which are of current interest and authors who are recognized as authorities in their respective fields. The list of monographs thus far secured appears in the publisher's own announcement elsewhere in this volume.

The development of knowledge in all branches of science, and especially in chemistry, has been so rapid during the last fifty years and the fields covered by this development have been so varied that it is difficult for any individual to keep in touch with the progress in branches of science outside his own specialty. In spite of the facilities for the examination of the literature given by Chemical Abstracts and such compendia as Beilstein's Handbuch der Organischen Chemie, Richter's Lexikon, Ostwald's Lehrbuch der Allgemeinen Chemie, Abegg's and Gmelin-Kraut's Handbuch der Anorganischen Chemie and the English and French Dictionaries of Chemistry, it often takes a great deal of time to coördinate the knowledge available upon a single topic. Consequently when men who have spent years in the study of important subjects are willing to coördinate their knowledge and present it in concise, readable form, they perform a service of the highest value to their fellow chemists.

It was with a clear recognition of the usefulness of reviews of this character that a Committee of the American Chemical Society recommended the publication of the two series of monographs under the auspices of the Society.

Two rather distinct purposes are to be served by these monographs. The first purpose, whose fulfilment will probably render to chemists in general the most important service, is to present the knowledge available upon the chosen topic in a readable form, intelligible to those whose activities may be along a wholly different line. Many chemists fail to realize how closely their investigations may be connected with other work which on the surface appears far afield from their own. These monographs will enable such men to form closer contact with the work of chemists in other lines of research. The second purpose is to promote research in the branch of science covered by the monograph, by furnishing a well digested survey of the progress already made in that field and by pointing out directions in which investigation needs to be extended. To facilitate the attainment of this purpose, it is intended to include extended references to the literature, which will enable anyone interested to follow up the subject in more detail. If the literature is so voluminous that a complete bibliography is impracticable, a critical selection will be made of those papers which are most important.

The publication of these books marks a distinct departure in the policy of the American Chemical Society inasmuch as it is a serious attempt to found an American chemical literature without primary regard to commercial considerations. The success of the venture will depend in large part upon the measure of coöperation which can be secured in the preparation of books dealing adequately with topics of general interest; it is earnestly hoped, therefore, that every member of the various organizations in the chemical and allied industries will recognize the importance of the enterprise and take sufficient interest to justify it.

Preface.

At the present time the field of organic arsenicals is probably the subject of more extensive chemical, biological and chemotherapeutic investigations than that of any other metal. This is dependent, in a large measure, upon the observations of the pioneers in this field, that carbon possesses a strong affinity for arsenic. As a result many satisfactory methods for the synthesis of organic arsenicals have been developed. The elaboration of these derivatives has also been greatly facilitated by the fact that it is often possible to isolate them in pure form—in many cases crystalline compounds are obtained.

For several centuries prior to 1900 there existed conflicting ideas regarding the practical value of arsenic in medicine, but all doubt as to its therapeutic efficiency was finally dispelled with the demonstration of striking curative effects produced by organic arsenicals. Among the earliest observations made with this class of compounds were those of Thomas, Breinl and Kinghorn, who in 1905 noted that atoxyl exerted a favorable influence in experimental trypanosomiasis. This led to the extensive investigations of Ehrlich and his collaborators, which culminated in the elaboration of arsphenamine and directed the attention of the scientific world to the field of organic arsenicals.

During the past ten years this branch of chemistry has developed at such a rate that treatises on the subject written only a few years ago seem now to be inadequate. The authors have felt for some time that a more modern book on arsenicals is necessary and, accordingly, we have written this monograph with the hope that it may serve to facilitate investigations in this field. It has been our aim to include practically every compound of this type reported in the literature up to date, and we have consulted almost all of the original articles and patents published in the English, German, French and Russian languages. With the exception of a few extremely important compounds and their intermediates, no detailed methods of preparation have been given because of lack of space. The list of references, however, in the back of the book was made as complete as possible in order to assist the investigator in finding details of the original work. The arsenicals without C — As linkage have not been treated as completely as the rest of the monograph because, strictly speaking, they do not lie within the scope of this work.

In order to acquaint the chemist with the significance of the organic arsenicals in medicine a special chapter on the chemotherapy of these compounds has been included. This may also be of value to the biologist

as it represents an attempt to treat chemotherapy as a distinct branch of medical science, and to describe its aims and the modern methods employed in chemotherapeutic investigations.

The authors are indebted to Mr. William R. Winicov, one of our associates at the Dermatological Research Laboratories, for his wholehearted coöperation and invaluable assistance both in the writing of this book and in its preparation for publication; to Dr. Jay F. Schamberg, Dr. John A. Kolmer, Dr. Alfred S. Burdick, and the Abbott Laboratories of Chicago for their encouragement and assistance; to Dr. Austin M. Patterson for his suggestions regarding the nomenclature, and to Mr. Barrett C. Fisher for his assistance in the reading of the proof. Finally, we desire to express our thanks to Mr. Asa Don Dickinson, librarian of the University of Pennsylvania, and to Mr. Alfred Rigling, librarian of the Franklin Institute of Philadelphia, for their kindness in granting us access to various journals in the above libraries.

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List of Abbreviations.

Amer. Chem. J.	American Chemical Journal
Am. J. Med. Sci.	The American Journal of the Medical Sciences
Am. J. Syphilis	The American Journal of Syphilis
Anales soc. chim.	Anales de la sociedad quimica Argentina
Ann.	Justus Liebig's Annalen der Chemie
Ann. chim.	Annales de chimie
Ann. chim. anal.	Annales de chimie analytique et revue de chimie analytique
Ann. inst. Pasteur	Annales de l'institut Pasteur
Apoth. Ztg.	Apotheker Zeitung
Arch. Derm. Syph.	Archives of Dermatology and Syphilology
Arch. exp. Path. Pharmakol.	Archiv für experimentelle Pathologie und Pharmakologie
Arch. farmacol. sper.	Archivio di farmacologia sperimentale e scienze affini
Arch. ital. biol.	Archives italliennes de biologie
Arch. Pharm.	Archiv der Pharmazie
Atti accad. Lincei	Atti della reale accademia dei Lincei
Ber.	Berichte der deutschen chemischen Gesellschaft
Berl. klin. Wochschr.	Berliner klinische Wochenschrift
Berz. Jahresber.	Berzelius' Jahresbericht
Biochem. J.	The Biochemical Journal
Biochem. Z.	Biochemische Zeitschrift
Boll. chim. farm.	Bolletino chimico-farmaceutico
Brit. Med. J.	British Medical Journal
Bull. acad. méd.	Bulletin de l'académie de médecine
Bull. soc. chim.	Bulletin de la société chimique de France
C. A.	Chemical Abstracts
Can. Chem. J.	Canadian Chemical Journal
Chem. News	Chemical News and Journal of Physical Science
Chem. Zentr.	Chemisches Zentralblatt
Clin. med. ital.	Clinica medica italiana

Compt. rend. .... Comptes rendus hebdomadaires séances de l'académie des sciences
Compt. rend. soc. biol. .... Comptes rendus des séances de la soci de biologie.
D. R. P. .... Deutsches Reichspatent
Deut. med. Wochschr. .... Deutsche medizinische Wochenschrift
Dissert. .... Dissertation
Eng. P. .... English Patent
Fr. P. .... French Patent
Gazz. chim. ital. .... Gazzetta chimica italiana
Giorn. chim. applicata ...... Giornale di chimica applicata
Giorn. farm. chim. .... Giornale di farmacia, di chimica e di s enze affini
Jahresber. .... Jahresberichte
Jahresber. Fort. Chem. ...... Jahresbericht über die Fortschritte c Chemie
J. Am. Chem. Soc. .... Journal of the American Chemical Socie
J. Am. Med. Assoc. .... The Journal of the American Medic Association
J. Biol. Chem. .... The Journal of Biological Chemistry
J. Chem. Soc. .... Journal of the Chemical Society (Londo
J. Exp. Med. .... The Journal of Experimental Medicine
J. Ind. and Eng. Chem. ...... The Journal of Industrial and Enginee ing Chemistry
J. Lab. Clin. Med. .... The Journal of Laboratory and Clinic Medicine
J. Pharmacol. .... Journal of Pharmacology and Experime tal Therapeutics
J. pharm. chim. .... Journal de pharmacie et de chimie
J. prakt. Chem. .... Journal für praktische Chemie
J. Russ. Phys. Chem. Soc. ... Journal of the Russian Physical-Chem cal Society
Med. Woche .... Medizinische Woche
Mem. Coll. Sci. Kyoto Imp. Univ. .... Memoirs of the College of Science, Kyot Imperial University
Mém. math. phys. .... Mémoires de mathematique et physiq des savants étrangers
Münch. med. Wochschr. .... Münchener medizinische Wochenschrift
Pharm. J. .... The Pharmaceutical Journal and Pha macist
Pharm. Post. .... Die oesterreichische Pharmazeutische Po

Pharm. Ztg. .... Pharmazeutische Zeitung
Pharm. Zentralhalle .... Pharmazeutische Zentralhalle für Deutschland
Pogg. Ann. .... Poggendorff's Annalen der Physik und Chemie
Proc. Roy. Soc. .... Proceedings of the Royal Society
Proc. Soc. Exptl. Biol. Med. ... Proceedings of the Society for Experimental Biology and Medicine
U. S. P. .... United States Patent
U. S. Public Health Rept. ... United States Public Health Report
Z. angew. Chem. .... Zeitschrift für angewandte Chemie
Z. Chemotherap. .... Zeitschrift für Chemotherapie
Z. Immunitäts. .... Zeitschrift für Immunitätsforchung und experimentelle Therapie
Z. physiol. Chem. .... Zeitschrift für physiologische Chemie (Hoppe-Seyler's)

ORGANIC ARSENICAL COMPOUNDS

Historical Sketch.

Although the number of known organic arsenicals now extends into the thousands, they are all synthetic products, with the possible exception of diethylarsine, which is claimed to be the gaseous product liberated by certain moulds from carpets or wall papers containing arsenical pigments.[1, 2, 3, 4] The first recorded observations of the production of an organic arsenic compound were made in 1760 by L. C. Cadet de Gassicourt,[5] who may be regarded as the father of this class of compounds. He distilled a mixture of equal parts by weight of arsenic trioxide and potassium acetate in a glass retort luted to a receiver of the same material, and obtained two liquids, one being volatile and exhibiting acidic properties, while the other less volatile product was a heavy, fuming liquid inflammable in the air and having an intensely disagreeable garlicky odor. The latter became known as "Cadet's fuming arsenical liquid." This experiment was repeated by de Morveau, Maret and Durande, who also separated the two liquids and confirmed Cadet's observations regarding the heavier substance. The spontaneous inflammability of the latter they attributed to a new compound formed by the union of the arsenic trioxide and potassium acetate. These noteworthy observations, however, failed to arouse much interest among the other chemists of that time; they were satisfied with the knowledge that it contained arsenic, and that it was either poisonous or at least very irritating to the throat.

It was not until 1804 that interest in Cadet's fuming liquid was revived. After some experimentation Thénard[6] concluded that it was a complex arsenical acetate containing partially deoxidized arsenic trioxide. Subsequently such prominent chemists as Berzelius, Laurent, J. B. Dumas and Gerhardt studied the same compound and evolved various theories as to its constitution without being able to confirm their ideas with experimental evidence. In 1837 Bunsen[7] began a systematic, quantitative study of Cadet's liquid, which lasted for a period of six years. He applied the name "alkarsin" to the above liquid, and regarded it as a polymeric alcohol with the oxygen replaced by an equal number of arsenic atoms, corresponding to the formula $As(CH_3)_2$. J. B. Dumas,[8]

working along the same lines, also concluded that alkarsin was a oxygen-free compound of the composition $C_4H_{12}As_2$, and sought to explain its formation by the action of acetic acid upon hydrogen arsenide.

After the appearance of Bunsen's first article, Berzelius became interested in this compound. He regarded alkarsin as the oxide of a compound radical $C_4H_{12}As_2$, which he named "kakodyl" on account of the disagreeable odor of its derivatives. Further light was thrown upon this subject when Bunsen [9] repeated his first experiments—this time with a carefully purified sample—and found that it contained oxygen and corresponded to the formula $C_4H_{12}As_2O$. He later described and determined the formulas of normal and basic cacodyl halides, the cyanide, sulfide, disulfide and selenide, double salts of cacodyl chloride and the halides of heavy metals, and similar compounds of cacodyl oxide.[10]

In 1842 Bunsen finally succeeded in isolating cacodyl by treating cacodyl chloride with zinc.[11] This was an event of great importance as it helped to clear up the composition of Cadet's fuming liquid. It was, however, of even greater significance at that time, when numerous attempts were being made to isolate compound radicals supposed to be capable of existence in accordance with the theory of Berzelius. The following year [12] he published the results of his investigation of cacodylic acid, hitherto designated as "alkargen." He ascribed to it the formula $C_4H_{14}As_2O_4$, and described several of its salts as well as some of the metallic salts of thiocacodylic acid. It is interesting to note that Bunsen also examined the physiological action of cacodyl and its derivatives.

The constitution of cacodyl now became the subject of considerable discussion. Frankland, who had discovered that zinc reacted with alkyl halides to form zinc dialkyls, regarded it as a compound of arsenic and the methyl radical. According to him its structure was analogous to that of arsenic disulfide, while cacodyl oxide and cacodylic acid corresponded to arsenic trioxide and arsenic acid respectively.[13] Kolbe considered cacodyl as a coupled radical consisting of two equivalents of methyl and one of arsenic, and hence was closely related to zinc and tin dialkyls.[14] It remained for Cahours and Riche [15] to definitely establish the correct constitution of cacodyl, which they obtained together with trimethylarsine and tetramethylarsonium iodide by the interaction of methyl iodide and sodium arsenide. They also showed that cacodyl reacts with alkyl halides according to the equation:

$$(CH_3)_2As-As(CH_3)_2 + 2RX \longrightarrow (CH_3)_2R_2AsX + (CH_3)_2AsX,$$

and that upon heating arsenic with alkyl iodides there are obtained double salts of tetraalkyl arsonium iodides and arsenic triiodide, e. g.,

$$2As + 4CH_3I \longrightarrow (CH_3)_4AsI.AsI_3.$$

The interest aroused in Cadet's liquid led other investigators to experiment along the same line by replacing potassium acetate with

salts of the higher homologous acids. Accordingly, in 1848 Wöhler[16] obtained inconclusive results on distilling equal parts by weight of arsenic trioxide and potassium butyrate, while five years later appeared the observations noted by Gibbs[17] on distilling white arsenic and potassium valerate. In 1854 Landolt[18] synthesized ethyl cacodyl by Cahours and Riche's method, employing ethyl iodide. He also prepared triethylarsine and ethylcacodylic acid, and showed that these ethyl derivatives corresponded with the cacodyl compounds in almost every respect.

The next important advance in the field of organic arsenicals was made by Baeyer.[19] In 1858 he distilled Cadet's liquid with concentrated hydrochloric acid and mercuric chloride, and obtained pure cacodyl chloride, which upon distillation with potassium hydroxide yielded pure cacodyl oxide. He also showed that cacodyl chloride was unsaturated by combining it with chlorine to form a trichloride which was identical with the compound prepared by Baeyer from cacodylic acid and phosphorus pentachloride. He further observed that the trichloride may be converted into cacodylic acid by hydrolysis; that warming at a moderate temperature decomposes it into methyl chloride and methyldichloroarsine, and that the latter can be employed as the starting material in the preparation of other arsenicals, such as methylarsinetetrachloride, methyldiiodoarsine, methylarsinesulfide and methylarsonic acid.

In 1859 Cahours[20] found that by heating alkyl iodides with zinc or cadmium arsenite, it was possible to obtain double salts of the arsonium iodide and the metallic iodide, e. g., $(CH_3)_4AsI.ZnI_2$ or CdI_2, from which the quaternary iodide could be isolated by treatment with aqueous caustic potash. He showed that this was a general method of preparing quaternary compounds, and that the latter could be converted into tertiary arsenicals by distillation either alone or over solid caustic potash. In addition, Cahours prepared tetramethyl- and tetraethylarsonium triiodides, compounds similar to the corresponding ammonium triiodides previously obtained by Weltzien. The arsonium triiodides, he found, could be decomposed by distillation into an alkyl iodide and a dialkyl iodoarsine; the latter, upon heating with iodine, could then be converted into the corresponding alkyl diiodoarsine, and this in turn into arsenic triiodide. He thus clearly showed the simple relationship existing among the four series of organic arsenicals:

$$RAsI_2,\ R_2AsI,\ R_3As,\ R_4AsI.$$

In 1861 Hofmann[21] prepared an interesting compound, triethyl-ω-bromoethylarsonium bromide, from which he obtained triethylvinylarsonium hydroxide and double salts of the corresponding chloride with platinic and gold chlorides. These were the first arsenicals to be prepared which contained an unsaturated radical. The same investigator also prepared diarsonium compounds,[22] e. g.,

$$(C_2H_5)_3\underset{\substack{|\\ Br}}{As}CH_2.CH_2\underset{\substack{|\\ Br}}{As}(C_2H_5)_3,$$

arsammonium salts,[23] e. g., $(C_2H_5)_3\underset{\substack{|\\ Br}}{As}CH_2.CH_2.\underset{\substack{|\\ Br}}{N}H_3$, and phosphoarsonium compounds,[24] e. g., $(C_2H_5)_3\underset{\substack{|\\ Br}}{As}CH_2.CH_2\underset{\substack{|\\ Br}}{P}(C_2H_5)_3$.

The next year Cahours[25] synthesized pentamethylarsine, the only arsenical ever prepared in which five alkyl or aryl radicals are attached to a single arsenic atom.

The investigations of Hofmann and Cahours mark the end of the first epoch in the history of organic arsenicals, during which time the pioneers in this field had dealt solely with aliphatic compounds. The distinction of preparing (though unknowingly) the first aromatic compound of arsenic belongs to Béchamp.[26] In 1860, while studying the conditions under which magenta is produced from aniline, he noted that aniline arsenate when heated with an excess of aniline did not yield colored products until a temperature of 190-200° had been reached. Three years later he described a colorless product which he had obtained by heating aniline arsenate under the above conditions.[27] He regarded this new substance as an acidic anilide of the formula $C_{12}H_8O_6AsN$; prepared its sodium, potassium, silver and barium salts, and concluded that it was a monobasic acid. Nothing further was said about this compound for the next forty years.

In 1875 Michaelis[28] began his investigation of aromatic arsenicals, which ultimately resulted in the synthesis of a large number of these compounds, embracing almost every type known at the present time. The first compound in this series was phenyldichloroarsine, which he obtained by heating mercury diphenyl and arsenic trichloride in a sealed tube, the reaction proceeding according to the equation:

$$Hg(C_6H_5)_2 + 2AsCl_3 \longrightarrow 2C_6H_5AsCl_2 + HgCl_2.$$

This method was generalized so that it became possible to obtain a series of aryl dihalogenated arsines. From the above dichloroarsine he then prepared the first pentavalent aromatic arsenical, phenylarsinetetrachloride.[29]

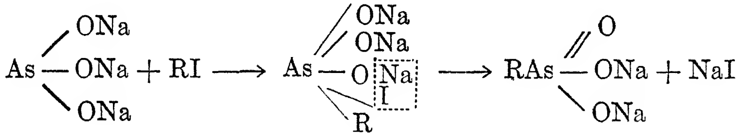
LaCoste[30] in 1881 noted that the methyl group of 4-methylphenylarsonic acid could be oxidized to a carboxyl by means of potassium permanganate in alkaline solution, forming a carboxyphenylarsonic (benzarsonic) acid. In the same year Michaelis and Schulte[31] prepared the first arseno compound, arsenobenzene, by reducing phenylarsineoxide with phosphorous acid in alcoholic solution. The following year they prepared the same compound by similarly reducing the correspond-

ing arsonic acid. This discovery was destined to be of the utmost importance to the domain of chemotherapy, as it was Ehrlich's observation of the trypanocidal and spirillicidal action of arseno compounds, that led to the elaboration of the remarkable drugs, arsphenamine and neoarsphenamine.

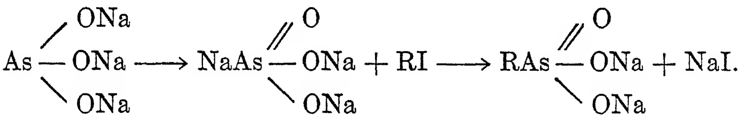
An important method of preparing tertiary aromatic arsines was developed by Michaelis and Reese [32] in 1882. It consists in treating a mixture of an aryl halide and arsenic trihalide with metallic sodium in the presence of a suitable anhydrous medium:

$$3RX + AsX_3 + 3Na_2 \longrightarrow R_3As + 6NaX.$$

In 1883, Meyer [33] developed a very interesting method of preparing primary aliphatic arsonic acids from sodium arsenite and alkyl iodides, the reaction proceeding according to either of the following equations:



or



This method, known as "Meyer's Reaction," was modified by Klinger and Kreutz [34] in 1889, and extended by Dehn [35] in 1905.

Up to 1894 the belief existed that arsenic, unlike nitrogen and phosphorus, could not form primary or secondary alkyl or aryl arsines. This theory was partially disproved when Palmer [36] succeeded in obtaining dimethylarsine from cacodyl chloride by reduction with platinized zinc and hydrochloric acid, and completely broken down seven years later when the same investigator, in collaboration with Dehn, prepared methyl- and phenylarsines.[37]

Partheil and Amort [38] obtained in 1898-9 a series of double salts of "hexaalkyldiarsonium" iodides and mercuric iodide by heating alkyl iodides with mercuric arsenide in a sealed tube. Mannheim repeated these experiments in 1905, and showed that the above compounds were in fact double salts of tetraalkylarsonium iodides and mercuric iodide.[39]

In 1902 there appeared two important articles by Michaelis [40] which, in addition to the description of a large number of arsenicals, contained a new general method for the preparation of primary dihalogenated arsines by heating tertiary arsines with arsenic trichloride in a sealed tube. Among the new compounds contained in these articles were naphthalene derivatives and tri(sulfophenyl)arsine oxide. The

latter was the only sulfonated arsenical prepared up to 1922, when Hill and Balls [41] isolated a sulfonaphthylarsonic acid.

In 1905 Dehn investigated Meyer's reaction for the preparation of alkyl arsonic acids, and found that better yields could be obtained by employing potassium arsenite instead of the sodium salt, and that alkyl iodides were better suited for this reaction than the bromides.[42] In the same paper he described ethylarsine and also various arsonium compounds prepared from ethyl- and phenylarsines and alkyl iodides according to the equation:

$$RAsH_2 + 3R'I \longrightarrow RR'_3AsI + 2HI.$$

The following year Dehn and Wilcox prepared the only known secondary aromatic arsine, diphenylarsine.[43] In the same year Dehn and McGrath [44] extended Meyer's reaction to the preparation of various other aliphatic arsonic acids, and also described the most favorable conditions for obtaining the best yields.

About this time the initial researches in the field of chemotherapy were begun. In 1903 Laveran found that although arsenious acid kills trypanosomes in the test-tube, it is incapable of destroying them in the animal body. In the same year Ehrlich, who together with Shiga had been conducting extensive investigations in the chemotherapy of trypanosome infections, undertook the study of atoxyl and observed that it did not exhibit any parasiticidal activity. In 1905, however, Thomas,[45] and in the following year Breinl and Kinghorn,[46] published papers in which they presented positive evidence that atoxyl has a therapeutic effect in experimental trypanosomiasis. Their results encouraged Ehrlich to such an extent that he again undertook the study of this compound, and also made plans for the preparation of new derivatives which might have a greater therapeutic effect and a lower toxicity. His initial difficulties were caused by the incorrect explanation of the constitution of atoxyl. As we have already seen, Béchamp had regarded his colorless product obtained from aniline and arsenic acid as an anilide of ortho arsenic acid whose structure, according to our modern notation, would correspond to the formula $C_6H_5\left(NHAs\begin{matrix} /\!\!/ O \\ - OH \\ \diagdown OH \end{matrix}\right)$. Since atoxyl was regarded as the monosodium salt of the above compound containing two molecules of water of crystallization, the possibility of producing new derivatives through the amino group seemed very remote. In addition, it was presumed that on account of the N-As linkage the arsenic acid radical would be easily split off by the usual hydrolyzing agents. Great was the surprise, therefore, when Ehrlich found that on treating atoxyl with nitrous acid there was obtained a substance which behaved like a diazo-compound and could be coupled with the usual azo components to form yellow, red or orange dyestuffs containing

arsenic. These reactions could not be reconciled with the accepted formula of atoxyl, which he and Bertheim soon proved to be incorrect, the true structure of the compound corresponding to a monosodium salt of para aminophenylarsonic acid. The free acid they named "arsanilic acid" on account of the similarity between its method of preparation and that of sulfanilic acid.

The recognition of the correct constitution of atoxyl proved to be of the utmost importance to chemotherapy, as it opened a wide field for chemical and biological investigation. Thus, by attacking the amino group, a large number of new compounds were prepared, among the first of which was 4-acetylaminophenylarsonic acid isolated by Ehrlich. Its sodium salt ("arsacetin") was superior to atoxyl in therapeutic value, but despite the occasional cures obtained with it in mice infected with trypanosomes, the results were not satisfactory, because of the uncertainty of its after-effects upon the animal. As both atoxyl and arsacetin exhibited no trypanocidal properties in the test-tube but exerted a therapeutic action when injected into the body, Ehrlich concluded that the drugs must undergo some change before they can effectively act upon the parasites. Now, in previous investigations, particularly on the "oxygen requirements of the body," Ehrlich had found that many tissues act as reducing substances. This prompted him to assume that pentavalent arsenicals, such as atoxyl and arsacetin, probably undergo reduction in the animal body before acting upon the trypanosomes. Accordingly, he reduced the arsonic acids to arseno compounds by means of suitable reducing agents, e. g., sodium hydrosulfite, and observed that the products were stronger trypanocidal agents. Among the first of these was arsenophenylglycine, a single injection of which was sufficient to sterilize experimental animals. At this time Ehrlich, in an address before the "Deutsche Chemische Gesellschaft," remarked that even if arsenophenylglycine, which had thus far exhibited the best results in animal experimentation, should not fulfill his expectations in human therapy, the way was clearly indicated—the reduction of the arsenical should not be left to the human body, but should be accomplished in the test-tube. By introducing suitable groups into the aromatic nucleus he hoped to diminish the toxicity of the arsenicals, from which number he would select those possessing the maximum affinity for the arsenic receptors. Accordingly, a series of new arsenicals were prepared and tested out upon experimental animals, among which were a number of amino arsonic acids, N-acylated derivatives of the same, di(4-aminophenyl)arsinic acid, hydroxy arsonic acids, 4-aminophenylarsineoxide and arseno compounds. The latter were found to possess the undesirable property of rapidly oxidizing in the air to form toxic compounds.

The problem was finally solved by utilizing the results obtained in other fields of research. While engaged in chemotherapeutic studies of azo dyestuffs, Ehrlich noted that compounds containing the hydroxyl

and amino groups in ortho position to each other were the most active in destroying trypanosomes. He applied this to the arsenicals, and with the assistance of his collaborators prepared among other products 4-oxalylaminophenylarsonic acid, 3-nitro-4-oxalylaminophenylarsonic acid, 3-nitro-4-aminophenylarsonic acid and 3-nitro-4-hydroxyphenylarsonic acid. By reducing the latter with sodium hydrosulfite they finally obtained 3,3′-diamino-4,4′-dihydroxyarsenobenzene and its dihydrochloride, which proved to be the best medicament in the treatment of syphilis. It was first known as "606" on account of the fact that 605 other preparations were made before its discoverers finally elaborated this most efficacious drug, which was marketed under the trade name "Salvarsan." Later a similar product was manufactured in England and named "Kharsivan"; also by the French who called it "Arsenobenzol," while in the United States the name "Arsphenamine" was adopted. The results obtained with this new drug exceeded all expectations, for not only trypanosomes, but also spirillæ and spirochetes were removed from the blood of the infected animals in a remarkably short time. Subsequent therapeutic investigations in syphilis, frambœsia, recurrent fever, etc., proved it to be the most valuable remedy yet produced for treating these diseases.

The work of Ehrlich and his co-workers did not terminate with the elaboration of arsphenamine—they continued their search for still more effective remedies. As a result, numerous derivatives of arsphenamine were prepared and investigated biologically, the most important of which was "Neosalvarsan," a product very easily soluble in water with a neutral reaction, and prepared from 3,3′-diamino-4,4′-dihydroxyarsenobenzene and sodium formaldehydesulfoxylate. Although this substance is not quite as therapeutically effective as arsphenamine, it has a lower toxicity and is tolerated much better by patients. The use of neoarsphenamine has been increasing continually, so that to-day it is the most widely employed arsenical in the treatment of syphilis.

The same investigators prepared various polyamino arseno compounds and several isomers of arsphenamine, which did not compare with the latter as a therapeutic agent. They also noted that the arseno compounds can be further reduced to arsines, compounds so easily oxidizable that they cannot find practical application in therapy, but are quite valuable in various syntheses. Thus, they react with arsineoxides to yield arseno compounds:

$$RAsH_2 + R'AsO \longrightarrow RAs = AsR' + H_2O.$$

If R and R′ are different radicals, the resulting products are unsymmetrical arseno compounds. The latter were also produced by the same investigators upon reducing a mixture of two different arsonic acids:

$$RAsO_3H_2 + R'AsO_3H_2 + 4H_2 \longrightarrow RAs = AsR' + 6H_2O;$$

or by the interaction of two different symmetrical arseno compounds:

$$RAs=AsR+R'As=AsR' \longrightarrow 2RAs=AsR'.$$

They also showed that the arsines could be condensed with aryl dihalogenated stibines or with bismuth trihalide to form arseno-stibino and arseno-bismuth compounds respectively:

$$RAsH_2+R'SbCl_2 \longrightarrow RAs=SbR'+2HCl$$

$$\begin{cases} RAsH_2+BiCl_3 \longrightarrow RAs=BiCl+2HCl \\ 2RAs=BiCl+RAsH_2 \longrightarrow RAs<\begin{matrix}Bi=AsR\\Bi=AsR\end{matrix}+2HCl \end{cases}$$

Finally, Ehrlich and his collaborators prepared various metallic coördination products of arseno compounds containing either one or two molecules of the metal, but the exact composition of these substances has not yet been definitely established. According to the followers of Ehrlich the metal attaches itself to the arsenic, the compounds corresponding to the formula $\begin{bmatrix} RAs\ldots Me \\ \| \\ RAs\ldots Me \end{bmatrix}\begin{matrix}X\\ \\X\end{matrix}$, where M = the metallic element and X the acid radical. On the other hand, Binz and his collaborators claim that arseno compounds containing no amino groups are unable to form coördination products with metallic salts, and that the metal must therefore be attached to the nitrogen. Thus, the substance obtained from arsphenamine and silver nitrate would be represented by the formula $\begin{matrix} AsC_6H_3(OH)(NH_2.AgCl) \\ \| \\ AsC_6H_3(OH)(NH_2.AgCl) \end{matrix}$. This discussion has recently assumed considerable importance on account of the appearance on the market of a new drug, silver arsphenamine, but no definite conclusions have thus far been reached.

Bertheim was not only the co-author of most of the papers published by Ehrlich on chemical subjects, but he also published a number of papers under his own name and in collaboration with others. In 1908 he described the preparation of an isomer of p-arsanilic acid by reducing Michaelis' nitrophenylarsonic acid, but he did not know whether the new acid was an ortho or a meta compound.[47] In the same year he obtained phenylarsonic acid, 4-hydroxy-, ethoxy-, chloro- and carboxyphenylarsonic acids from p-arsanilic acid by diazotizing and treating as in the case of non-arsenated aromatic amines.[48] In 1910 he prepared various nuclear halogenated derivatives of p-arsanilic acid;[49] in 1911 he described various derivatives of 4-aminophenylarsineoxide,[50] 4-oxalylaminophenylarsonic acid, 3-nitro-4-aminophenylarsonic acid, 3,4-diaminophenylarsonic acid and various derivatives of the latter,[51] and, together with Benda,[52] demonstrated that in Michaelis' nitrophenylarsonic acid the nitro group was in the meta position to the arsenic. In the following year appeared the account of his further studies on

3-amino-4-hydroxyphenylarsonic acid, in which were described compounds containing one, two and three methyl groups attached to the nitrogen, and their corresponding arseno derivatives.[53] In his next article on arsenicals, which appeared in 1914, he described his discovery that upon heating an arseno compound with methyl iodide in a sealed tube the following reaction takes place:

$$RAs = AsR + 3CH_3I \longrightarrow R(CH_3)_3AsI + RAsI_2.^{54}$$

In the succeeding year his last article was published posthumously.[55] It deals with the extension of Meyer's reaction to the preparation of aliphatic-aromatic arsinic acids by treating an aryl arsineoxide with an alkyl iodide in alkaline solution:

$$RAsO + R'X + NaOH \longrightarrow RR'AsO.OH + NaX \text{ (R = an aryl and R' an alkyl radical).}$$

Benda, one of the later collaborators of Ehrlich, prepared in 1908 a number of amino aryl arsonic acids and their derivatives by Béchamp's method. In these investigations he was assisted by Kahn.[56] In the same year he described for the first time di(4-aminophenyl)arsinic acid, di(3-methyl-4-aminophenyl)arsinic acid, their acetyl derivatives, di(4-hydroxyphenyl)arsinic acid and di(3-methyl-4-aminophenyl)arsinic acid.[57] In the following year he succeeded in obtaining amino aryl arsonic acids in which the amino group is ortho to the arsenic by heating para substituted amines with arsenic acid.[58] In 1911 he described 2,5-diaminophenylarsonic acid and showed that it could be converted into m-arsanilic acid.[59] In the same year he prepared for the first time o-arsanilic acid and several of its derivatives;[60] obtained 3-nitro-4-hydroxyphenylarsonic acid from 3-nitro-4-aminophenylarsonic acid by heating with caustic potash,[61] and described the conversion of 3-nitro-4-aminophenylarsonic acid into 4-amino-3-hydroxyphenylarsonic acid, from which he obtained an isomer of arsphenamine, 4,4'-diamino-3,3'-dihydroxyarsenobenzene.[62] In 1912 he showed that upon nitrating p-arsanilic acid under the proper conditions there results a 3,5-dinitro derivative whose amino group may be replaced by a hydroxyl on warming with aqueous caustic potash.[63] Two years later he described the first methoxy amino aryl arsonic acid, 3-methoxy-4-aminophenylarsonic acid, and various derivatives of the same,[64] also the preparation of 3,4,5-triaminophenylarsonic acid by reducing 3,5-dinitro-p-arsanilic acid.[65] Finally, in 1917 he prepared for the first time a number of arsenical derivatives of anthraquinone.[66]

The first publication on arsenicals by Karrer, another disciple of Ehrlich, appeared in 1912, and contains a description of 4-nitrosophenylarsonic acid.[67] The following year he described diazimidophenylarsonic acid, its various nuclear substituted derivatives, 3,4-dinitrosophenylarsonic acid and several phenazine dyes containing arsenic.[68] In the

same year he showed that 3-nitro-4-hydroxyphenylarsonic acid can be prepared from 3-nitro-4-dimethylaminophenylarsonic acid by heating with concentrated aqueous caustic soda.[69] In 1914 he was the first to describe 4-iodochloride-, iodoso- and iodoxyphenylarsonic acids,[70] and the method of converting 3,5-dichloro-4-aminophenylarsonic acid into 3,5-dichlorophenylarsonic acid, 3,5-dichloro-4-iodophenylarsonic acid, 3,5-dichloro-4-diazimidophenylarsonic acid and 5,5′-dichloro-4,4′-diamino-3,3′-dihydroxyarsenobenzene.[71] He observed an interesting phenomenon in connection with 2-nitrophenyldichloroarsine, namely, that when its solution in hydrous ether is preserved in a sealed tube exposed to direct sunlight it seems to change successively into 2-nitrophenylarsineoxide, 2-nitrosophenylarsinedioxide and 2-nitrophenylarsonic acid.[72] He also claimed that arsenicals containing two amino groups in meta position to each other dissolve in soda or sodium bicarbonate in the presence of free carbon dioxide, forming carbamino derivatives.[73] In the following year appeared his important article dealing with stilbene arsenicals,[74] and also one in which are described various carboxylated arsenicals, whose carboxy groups are in ortho position to the arsenic.[75] Later in the same year, in conjunction with Ehrlich, he published an article on the constitution of the arseno-metallic coördination products, in which was expressed the view that the metal is attached to the arsenic.[76] In 1916 he described a third method of preparing unsymmetrical arseno compounds by the interaction of two different symmetrical arseno derivatives.[77] Finally, in 1919 appeared his most recent article on arsenicals,[78] in which he offers further evidence in confirmation of his original view as to the constitution of the metallic coördination products of arseno compounds.

Following the elucidation of the chemical constitution of atoxyl, Pyman and Reynolds in 1908 prepared other amino aryl arsonic and arsinic acids by the Béchamp reaction.[79] In the same year Barrowcliff, Pyman and Remfry converted the above amino compounds into hydroxy derivatives by diazotizing and subsequently proceeding in the usual manner; they coupled the diazo compounds with various phenolic and amino compounds; and also prepared phenazine diarsonic acids by treating a dilute sulfuric acid solution of an amino aryl arsonic acid with ammonium persulfate.[80] In the same year Dehn[81] published the results of his further study of organic arsines. This article contained the first descriptions of diisoamylarsine, benzylarsine, diisoamyldimethylcacodyl and also several new aliphatic arsonium compounds which he obtained from secondary arsines and alkyl iodides:

$$R_2AsH + 2R'I \longrightarrow R_2R'_2AsI + HI$$

At this time Michaelis developed a very satisfactory method of preparing 4-dimethylaminophenylarsonic acid from the corresponding arsineoxide by oxidation with hydrogen peroxide in alkaline solution.[82] This

method was subsequently generalized. In 1908 Morgan and Micklethwait prepared dicamphorylarsinic acid and its oxychloride,[83] and the next year they isolated tricamphorylarsine dihydroxide.[84] At the same time Mameli found that o-nitroaniline could be arsenated directly by the Béchamp reaction.[85]

A very valuable general method for synthesizing aromatic arsonic and arsinic acids was developed by Bart in 1912.[86] The arsonic acids are obtained by diazotizing an amine, coupling with sodium arsenite, and warming until the nitrogen is completely removed:

$$RN = NX + Na_3AsO_3 \longrightarrow RAs\begin{cases} \overset{}{=}O \\ -ONa \\ -ONa \end{cases} + NaX + N_2.$$

If, however, the diazo compound is coupled with an aryl arsenite, the product is a diaryl arsinic acid:

$$RN = NX + R'As\begin{cases} ONa \\ ONa \end{cases} \longrightarrow RR'As\begin{cases} =O \\ -ONa \end{cases} + NaX + N_2.$$

This procedure, known as "Bart's Reaction," has been found very efficient in preparing new arsenicals, and has facilitated the preparation of many compounds already known. The method was later modified by Bart, who at first discovered that the alkaline medium can be dispensed with if copper salts are present,[87] and then subsequently obtained still better results with various metallic catalysts in alkaline solution.[88] In 1919 Mouneyrat modified Bart's method of synthesizing arsonic acids by causing normal diazo compounds to react with cold or warm, aqueous or dilute alcoholic solutions of arsenious acid in an acid, alkaline or neutral medium, and in the presence of special catalysts depending upon the particular medium selected.[89] The following year H. Schmidt [90] claimed that Bart's reaction proceeded most smoothly on treating normal diazo compounds with potassium arsenite in neutral or slightly acid medium without the aid of a catalyst.

Fourneau and Oechslin in 1912 prepared the stovaine and several interesting alkaloid esters of p-benzarsonic acid as well as their corresponding arseno derivatives.[91] In the same year Winmill attempted to resolve several arsonium compounds containing asymmetric arsenic atoms into optically active components, but obtained no striking results.[92]

In 1913 Fränkel and Löwy succeeded in preparing quinaldinearsonic acid by condensing p-arsanilic acid with acetaldehyde. They also described the corresponding arsineoxide.[93] About the same time Michaelis and Schäfer determined the molecular weights of arsenobenzene and p-arsenotoluene, and found them to correspond with the formulas $C_6H_5As = AsC_6H_5$ and $C_7H_7As = AsC_7H_7$ respectively, thereby further

demonstrating the structural similarity between arseno and azo compounds.[94] In the same year Danysz [95] observed that by employing a combination of arsphenamine and silver nitrate in the treatment of experimental trypanosomiasis, better therapeutic results can be obtained than with arsphenamine alone. In the following year he described three new compounds, prepared by combining arsphenamine with silver chloride, bromide and iodide,[96] and finally a triple combination of arsphenamine, silver bromide and trivalent antimony, which was introduced into therapy under the name of "Luargol." [97] In 1914 E. Fischer announced that the higher fatty acids of the acetylene series, e. g., behenolic or stearolic acid, when heated with arsenic trihalides, combine to form acid compounds containing arsenic. The best known of these is chloroarsinosobehenolic acid, whose strontium salt has been introduced into therapy under the name of "Elarson." [98] In the same year K. Oechslin prepared arsonic acids of the type $H_2O_3AsRN < {R' \atop CH_2COOR''}$ by heating N-phenylalkylglycine esters with arsenic trichloride in the presence of pyridine, and oxidizing with hydrogen peroxide. The corresponding arsinic acids are also formed at the same time. He also saponified the above arsonic acid esters and reduced the resulting acids to arseno derivatives. By applying this method to monoalkylated aryl amines he obtained alkylated amino arsonic and the corresponding arsinic acids.[99]

A valuable method of synthesizing dihalogenated arsines was developed by Roeder and Blasi [100] in 1914. It depends upon the treatment of arsenic trihalides with a mercurihalide of the type RHgX, where R represents an aliphatic, aromatic or heterocyclic radical, the reaction proceeding according to the equation:

$$RHgX + AsX_3 \longrightarrow RAsX_2 + HgX_2.$$

If the aromatic or heterocyclic mercurihalide contains groups capable of reacting with the arsenic trihalide, e. g., COOH, OH, NH_2, etc., they must first be protected by alkylation, as otherwise the haloid acid formed will split off the mercury.

In 1915 Finzi [101] prepared the first arsenical derivatives of thiophene by reacting arsenic trichloride with mercurydithienyl, or better with thienylmercurichloride, and oxidizing the resulting thiophene-2-dichloroarsine to the corresponding arsonic acid by means of hydrogen peroxide in alkaline solution. He also isolated the corresponding arsineoxide and 2,2′-dithienylarsinic acid. In collaboration with Furlotti [102] he also prepared 5-nitrothienyl-2-arsonic acid, the corresponding amino and acetylamino derivatives, and di(5-nitrothienyl)arsinic acid. At this time Grüttner and Wiernik [103] described two methods of preparing arylcyclopentamethylene arsines, the reactions proceeding according to the equations:

$$CH_2 < \begin{matrix} CH_2.CH_2.MgBr \\ CH_2.CH_2.MgBr \end{matrix} + \begin{matrix} Cl \\ Cl \end{matrix} > AsC_6H_5 \longrightarrow$$

$$CH_2 < \begin{matrix} CH_2.CH_2 \\ CH_2.CH_2 \end{matrix} > AsC_6H_5 + MgCl_2 + MgBr_2,$$

and

$$CH_2 < \begin{matrix} CH_2.CH_2.Br \\ CH_2.CH_2.Br \end{matrix} + 4Na + \begin{matrix} Cl \\ Cl \end{matrix} > AsC_6H_5 \longrightarrow$$

$$(CH_2)_5 = AsC_6H_5 + 2NaCl + 2NaBr.$$

The same investigators also described several derivatives of the above arsines containing pentavalent arsenic. In the following year Grüttner and Krause [104] obtained phenylcyclotetramethylenearsine and derivatives similar to those described under the pentamethylene compounds.

In 1915 appeared an article by Michaelis in which were described o- and p-arsenobenzoic acids.[105] This publication marked the conclusion of Michaelis' investigations in the field of organic arsenicals. He was the first deliberately to prepare aromatic arsenicals, of which he prepared a greater number than any other investigator up to the present time. Some of his methods of synthesis are still being used. As a result of his personal investigations and those in collaboration with his assistants, the chemistry of the aromatic arsenicals was placed on a firm foundation, and the way cleared for future triumphs in the new science, chemotherapy.

In 1916 Sieburg [106] described several higher aliphatic esters of 4-arsinoxybenzoic acid, arsinoxy compounds derived from 4-dichloroarsinobenzoyl chloride and various aliphatic and aromatic amino acids in alkaline solution, their corresponding arsonic acids and arseno derivatives. In the same year Zappi described methylcyclopentamethylenearsine (Methylarsepidine) and some of its derivatives.[107]

Steinkopf and Bauermeister in 1917 described a method of separating thienyl-2-dichloroarsine, 2,2′-dithienylchloroarsine and 2,2′,2″-trithienylarsine from the mixture obtained by reacting arsenic trichloride with mercurydithienyl or thiophenemercurihalide.[108] In 1920 Steinkopf in collaboration with Mieg [109] first prepared isoamyldichloroarsine, phenylmethylchloroarsine and ethylarsineoxide; obtained α-naphthyldichloroarsine and cacodyl chloride in pure form, and described the first thiocyanoarsines, the cacodyl- and diphenyl derivatives. In the following year, Steinkopf with various collaborators published five additional articles dealing with arsenicals. With Müller [110] he prepared triethylarsine cyanobromide by condensing triethylarsine and cyanogen bromide in the complete absence of moisture, which readily converts the addition product into triethylarsine hydroxybromide. He noted that in the above arsine cyanobromide the negative CNBr group has a greater affinity for arsenic than for the nitrogen of the corresponding amine derivative. He also prepared a similar cyanobromide with phenylcyclopenta-

methylenearsine.[111] With the coöperation of Schwen[112] he explained the simultaneous formation of arsonium iodides and triiodides by the interaction of aromatic arseno compounds and methyl iodide in the following manner:

$$\left\{\begin{array}{l} RAs=AsR \xrightarrow{CH_3I} \underset{CH_3\quad\ \ I}{R-As-AsR} \xrightarrow{CH_3I} {}^{R}_{CH_3}\!\!>\underset{I}{As}-\underset{I}{As}\!<^{R}_{CH_3} \\ \qquad\longrightarrow 2RCH_3AsI \xrightarrow{4CH_3I} 2R(CH_3)_3AsI_3; \\ 2R(CH_3)_3AsI_3 + RAs=AsR \longrightarrow R(CH_3)_3AsI + 2RAsI_2; \end{array}\right.$$

showed that a similar reaction occurs between cacodyl and an excess of methyl iodide:

$$(CH_3)_2As-As(CH_3)_2 \xrightarrow{CH_3I} \underset{I}{(CH_3)_2As} \vdots \underset{CH_3}{As(CH_3)_2} \longrightarrow$$

$$(CH_3)_2AsI + (CH_3)_3As \xrightarrow{3CH_3I} (CH_3)_4AsI_3 + (CH_3)_4AsI;$$

that secondary iodo arsines and methyl iodide combine to form arsonium triiodides:

$$R_2AsI + 2CH_3I \longrightarrow R_2(CH_3)_2AsI_3;$$

and that secondary chloro-, bromo- or cyanoarsines yield with methyl iodide a mixture of an arsonium monoiodide and triiodide, while cacodyl bromide and methyl bromide interact to form trimethylarsine dibromide:

$$(CH_3)_2AsBr + CH_3Br \longrightarrow (CH_3)_3AsBr_2.$$

The same authors obtained tetramethylarsonium iodide and phenyldiiodoarsine from tetramethylarsonium triiodide and symm. diphenyldiiododiarsine:

$${}^{C_6H_5}_{\ \ I}\!>As-As<^{C_6H_5}_{I} + (CH_3)_4AsI_3 \longrightarrow (CH_3)_4AsI + 2C_6H_5AsI_2,$$

and also diphenyldimethylarsonium enneaiodide, $(C_6H_5)_2(CH_3)_2AsI.I_8$, from the corresponding triiodide and iodine in a saturated alcoholic iodine solution. In subsequent articles these two investigators described several new tertiary aliphatic-aromatic arsine cyanobromides, hydroxy halides and picrates;[113] the results of their studies on the pyrogenic decomposition of tertiary aliphatic-aromatic arsine hydroxybromides,[114] and also several addition products of iodoform and arsonium halides.[115] The most recent work of Steinkopf, in collaboration with Donat and Jaeger, was published in 1922,[116] and deals with further studies of addition products of cyanogen bromide and tertiary arsines, including ethyl-

cyclopentamethylenearsine. In the same article the authors describe several new tertiary arsines, their hydroxy bromides and picrates, and dialkylcyclopentamethylenearsonium halides.

In 1918 Zappi and Landaburu [117] described several new salts of As-dimethylarsepidine which they had prepared from the corresponding hydroxide by treatment with mineral acids. In the same year Jacobs and Heidelberger utilized Bart's method for the preparation of a number of hitherto undescribed nitro aryl arsonic acids. They also devised a method of reducing these to the corresponding amino compounds by means of ferrous sulfate in alkaline medium.[118] In the following year they published the results of their studies on the action of arsenic acid upon phenol, in which they demonstrated that the action is more complicated than had been heretofore assumed, and that in addition to 4-hydroxyphenylarsonic acid there are also formed the ortho and meta isomers, di(2-hydroxyphenyl)arsinic acid and 2,4′-di(hydroxyphenyl)-arsinic acid. Thus, they were the first to prepare o- and m-hydroxyphenylarsonic acids, the identity of which they proved by synthesizing the same compounds from the corresponding amino acids by diazotizing and replacing the diazo group with a hydroxyl in the usual manner.[119]

In 1919 Raiziss [120] described a number of aryl arsonic acids containing nuclear mercury. The next year the same investigator published the results of his studies on the chemistry of arsphenamine and its relation to toxicity,[121] while in 1921 there appeared a similar article on neoarsphenamine,[122] demonstrating that the commercial drug is a non-uniform mixture of the mono and di-N-methylenesulfinic acid derivatives of arsphenamine together with uncombined sodium formaldehydesulfoxylate, sodium sulfate and chloride. In 1922 Raiziss, after a series of diffusion experiments with arsphenamine and some of its metallic coördination products, came to the conclusion that the latter are not homogeneous substances, as Bauer had claimed, but intimate mixtures of arsphenamine and the metals in colloidal form.[123] In the same year [124] he also described several condensation products of arsphenamine and various aldehydes of the type,

$$[RCH(OH)NH](HO)C_6H_3As = AsC_6H_3(OH)[NH(HO)HCR].$$

In 1919 Jacobs and Heidelberger outlined a plan of procedure for the synthesis of arsenicals for chemotherapeutic research.[125] They first prepared amides and alkyl amides of N-arylglycinearsonic acids by the interaction of sodium amino aryl arsonates with the amides or alkyl amides of chloro fatty acids: [126]

$$H_2O_3AsRNH_2 + ClCH_2CONHR' \longrightarrow$$
$$H_2O_3AsRNHCH_2CONHR' + HCl.$$

The most important compound of this series is N-(phenyl-4-arsonic acid)glycineamide or "Tryparsamide," $H_2O_3AsC_6H_4NHCH_2CONH_2$. In

a similar manner they obtained ureides and β-substituted ureides of N-arylglycinearsonic acids.[127] With chloroacetylurea or its simpler β-alkyl derivatives the reaction could be accomplished by boiling in aqueous solution with the sodium amino arylarsonates. In the preparation of the β-arylureides of phenylglycinearsonic acid, however, involving the use of the very sparingly soluble chloroacetyl-substituted phenylureas, the reaction proceeded most satisfactorily in 50 per cent. alcohol and only after sodium iodide had been added to bring about the intermediate formation of the more reactive iodoacetyl compounds. In the succeeding papers they described a number of aromatic amides of N-arylglycinearsonic acids,[128] also N-substituted glycylarsanilic acids,[129] N-(phenyl-4-arsonic acid)-α-phenylglycine and its amides,[130] substituted benzyl, phenoxyethyl and phenacylarsanilic acids,[131] the amides of (4-arsonic acid)-phenoxyacetic acid and the isomeric phenoxyacetylarsanilic acids,[132] diazoamino compounds of p-arsanilic acid and its derivatives,[133] and finally azo dyes derived from arsanilic acid.[134]

A study of the composition of commercial arsphenamine was made in 1920 by Fargher and Pyman who found that samples of the drug precipitated from methyl alcoholic solution by means of ether contain no methyl alcohol of crystallization. They also found that when the drug is prepared from 3-nitro-4-hydroxyphenylarsonic acid by reduction with sodium hydrosulfite, it contains from 1 to 3 per cent. of sulfur, of which one part is in the form of the group $—NH.SO_3H$, another part is attached to the arsenic, while the remainder is probably physically associated with the compound.[135] In the same year Burrows and Turner made the interesting observation that tertiary aliphatic-aromatic arsines combine additively with methyl-, ethyl- or phenyldiiodoarsine, to form compounds of the type $R_3As.R'AsI_2$, which may be separated into their constituents by dissolving in benzene.[136] In the following year the same investigators described several arsenicals containing asymmetric arsenic atoms. These compounds they found to be resolvable into optically active components, which, however, racemized so rapidly that the observed rotation was small.[137] Later in the same year they described additional products of phenyldimethylarsine with the iodides of phosphorus, arsenic, antimony, bismuth and quadrivalent tin, also similar products from phenyltrimethylarsonium iodide and the iodides of cadmium, lead and bivalent mercury.[138]

The question of sulfur in commercial arsphenamine was again investigated in 1921 by King,[139] who claims that the principal sulfur-containing impurities are the hydrochloride of 5-sulfo-3,3′-diamino-4,4′-dihydroxyarsenobenzene, $(HCl.H_2N)(HO)C_6H_3As = AsC_6H_2(OH)(NH_2)(SO_3H)$, and arsphenamine sulfate. In the same year Christiansen investigated the indirect reduction of 3-amino-4-hydroxyphenylarsonic acid to arsphenamine; suggested a method of preparing a relatively non-toxic sample of the latter, and described a polyarsenide of arsphenamine.[140] Later

he showed that a relationship exists between the toxicity and the mode of synthesis of arsphenamine.[141] Thus, by altering the conditions under which the nitro group of 3-nitro-4-hydroxyphenylarsonic acid is reduced, the toxicity of the product can be made to fluctuate within wide limits. Arsphenamine of comparatively low toxicity and sulfur content, he found, is more consistently obtained by using pure 3-amino-4-hydroxyphenylarsonic acid as the starting material. In addition, he noted that the relatively toxic by-products with a high sulfur content, formed during the preparation of the drug from 3-nitro-4-hydroxyphenylarsonic acid, are not due to impurities in the commercial sodium hydrosulfite.[142]

In 1921 Wieland and Rheinheimer described a long series of phenarsazine compounds.[143] About the same time Kalb published an account of the preparation of arsanthrene (diphenylenediarsine) and a number of its derivatives,[144] while Green and Price described β-chlorovinyldichloroarsine, di(β-chlorovinyl)chloroarsine and tri(β-chlorovinyl) arsine[145] which they obtained by the interaction of dry acetylene and arsenic trichloride in the presence of aluminium chloride. In the same year W. Lee Lewis published three articles on arsenicals. In the first,[146] he described 6-chlorophenoxarsine and a number of its derivatives, and pointed out the close resemblance between the chemical properties of the parent compound and those of diphenylchloroarsine; in the second, he described a method of condensing 4-dichloroarsinobenzoyl chloride with benzene, toluene, anisole, phenetole and diphenyl ether in the presence of aluminium chloride, with carbon bisulfide as a solvent,[147] while the third paper contained an account of 7-chloro-7,12-dihydro-γ-benzophenarsazine, prepared by condensing phenyl-α-naphthylamine with arsenic trichloride, and also a number of its derivatives.[148]

In 1922 Roger Adams published the results of his extensive investigations of various arsenical compounds. By employing alkyl bromides or chlorides instead of the iodides, he eliminated several objectionable features connected with the isolation of alkyl arsonic acids prepared by Meyer's reaction. He also prepared various aliphatic and mixed aliphatic-aromatic arsinic acids by a further application of the same reaction, employing alkyl halides and sodium alkyl or aryl arsenites respectively. By the same method he was also able to obtain many compounds of the general formula HO_2AsRCH_2CONHR', where R is a phenyl, 4-aminophenyl or 4-acetylaminophenyl group, and R′ is a phenyl or substituted phenyl group.[149] In a second article he showed that primary aryl arsines and aldehydes may react in three ways, depending upon the conditions of the experiment, forming bis(α-hydroxyalkyl)-arylarsines, tetrahydro-1,4,2,5-dioxdiarsines or arseno compounds,[150] while in a subsequent paper[151] he described 1-(4′-arsonophenyl)-2-phenyl-4,5-diketopyrrolidine and a number of derivatives of this series which he obtained by the action of pyruvic acid upon amino arylarsonic acids and aromatic aldehydes. He also found that those of the above

amino acids which contain substituents in ortho position to the amino group form benzylidene derivatives which do not react further with the pyruvic acid.

The importance of the impulse given by Ehrlich to the development of chemotherapy in general and to the expansion of the field of organic arsenicals in particular cannot be overestimated. The interest in these two sciences has penetrated all the civilized countries, where physicians, chemists, bacteriologists and protozoölogists are now united in their search for specifics of even greater therapeutic value than arsphenamine to aid humanity in its struggle against such dreaded diseases as cancer, tuberculosis, etc., which either entirely resist or are only slightly affected by the therapeutic agents now at our disposal.

Chapter I. Trivalent Aliphatic Arsenicals.

A. Primary Derivatives.

1. *Alkyl Arsines,* $RAsH_2$.—Unlike the corresponding amines and phosphines, the members of this group are practically devoid of basic properties, with the exception of ethylarsine which combines with sulfuric acid to form a salt easily decomposed by water. They are prepared by reducing primary arsonic acids with amalgamated zinc dust and hydrochloric acid in alcoholic medium, with the exclusion of atmospheric oxygen. The pure products, obtained by distilling under reduced pressure, are colorless, mobile, transparent oils of high refractive power, readily soluble in alcohol or ether, slightly so in water, and possessing disagreeable odors and powerfully virulent properties. In contrast with arsine (AsH_3), they readily absorb oxygen from the air, the affinity for this element increasing with the number of alkyl groups attached to the arsenic. Thus, methylarsine is first partially oxidized to methylarsine-oxide, which then reacts with the remaining arsine to form a glistening red polymer of arsenomethane, $(CH_3As)_4$; ethylarsine yields a light-yellow substance, while the secondary and tertiary arsines spontaneously inflame in the air, the former yielding dialkylarsinic acids, $R_2AsO.OH$, and the latter trialkylarsine oxides, R_3AsO. Dilute nitric acid oxidizes the primary arsines to alkylarsonic acids, but the concentrated reagent decomposes them, oxidizing the alkyl groups to the corresponding fatty acids, and the arsenic to a mixture of arsenic- and arsenious acids. They are also oxidized to arsonic acids by silver nitrate. Dry halogens react with the primary arsines to form alkyldihalogenated arsines, the reaction probably proceeding as follows:

$$RAsH_2 + X_2 \longrightarrow RAsHX.HX \longrightarrow RAsHX + HX$$
$$RAsHX + X_2 \longrightarrow RAsX_2.HX \longrightarrow RAsX_2 + HX$$

In the presence of a solvent, however, oxidation to the arsonic acid occurs.

When heated with alkyl halides in a sealed tube at 110°, the arsines react to form arsonium compounds:

$$CH_3AsH_2 + 3CH_3I \longrightarrow (CH_3)_4AsI + 2HI.$$

At ordinary temperature, however, there are obtained white or slightly yellow, iridescent crystals which are stable in dry air, but are decomposed by moisture with the simultaneous manifestation of a cacodyl

odor. No analyses of these compounds have been made, but they probably correspond to the formula $R_2AsH.HI$. By heating the arsines in sealed tubes at high temperatures, they decompose into the respective hydrocarbons, metallic arsenic and hydrogen; with ethylarsine a second reaction evidently occurs, as triethylarsine is also produced.

Methylarsine, CH_3AsH_2.—Sodium methylarsonate and an excess of amalgamated zinc dust are introduced into a large flask and treated with the proper amount of hydrochloric acid diluted with an equal volume of alcohol. The generator is connected in series with a wash bottle containing water, a long drying tube filled with soda lime, and a

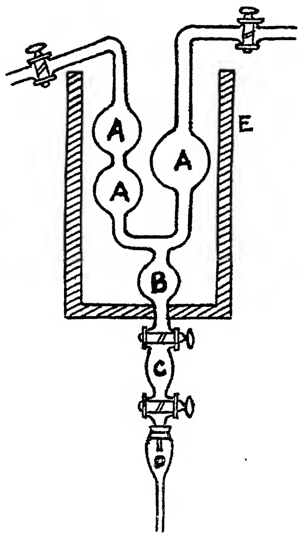


Fig. 1

condenser of special form, fixed in a wooden vessel charged with solid carbon dioxide or a freezing mixture of ice and salt as shown in Figure 1. Its exit tube is connected with two wash bottles, the first containing concentrated sulfuric acid to exclude moisture, and the second concentrated nitric acid to destroy any uncondensed arsine. All connections must be made by sealing the glass together as rubber is rapidly attacked. Air must be excluded from the entire apparatus at the beginning of and during the reduction.

The condensed arsine is collected in the receiver (D) filled with hydrogen and preserved in sealed tubes.[152] It is a colorless, transparent mobile liquid of high refractive power, b. p. 2°/755 mm., 17°/1.5 atmos.; soluble in alcohol, ether or carbon bisulfide, but very sparingly in water. The arsine has a disagreeable, penetrating odor like that of cacodyl, is

very poisonous, and fumes in the air, but is not spontaneously inflammable. It exhibits but very feebly basic properties, combining only to a very slight extent with hydrogen chloride under ordinary temperature and pressure, even after standing for a period of two weeks. It is oxidized by iodine solution to methylarsonic acid:

$$CH_3AsH_2 + 6I + 3H_2O \longrightarrow CH_3AsO(OH)_2 + 6HI.$$

On standing over mercury in contact with pure, dry oxygen, it is rapidly converted into the arsineoxide:

$$CH_3AsH_2 + O_2 \longrightarrow CH_3AsO + H_2O;$$

upon continued standing, however, further oxidation to the arsonic acid occurs:

$$CH_3AsO + O + H_2O \longrightarrow CH_3AsO(OH)_2.$$

The last oxidation can be prevented by removing the water formed in the first phase of the reaction by means of fused calcium chloride.

With concentrated nitric acid the arsine yields methylarsonic, formic and arsenic acids; with mercuric chloride, mercuric methylarsonate is formed, while in a neutral or alkaline solution of silver nitrate, oxidation to the arsonic acid occurs. By decolorizing an alcoholic solution of iodine with methylarsine and evaporating the resulting solution to dryness, amber-colored needles of methyldiiodoarsine separate:

$$CH_3AsH_2 + 2I_2 \longrightarrow CH_3AsI_2 + 2HI;$$

but an excess of arsine produces an unidentified, brown, amorphous mass. Bromine in carbon bisulfide solution decomposes the arsine thus:

$$CH_3AsH_2 + 6Br \longrightarrow AsBr_3 + 2HBr + CH_3Br;$$

with concentrated hydriodic acid methyldiiodoarsine results; with hydrogen sulfide there is a slight formation of methylarsinesulfide:

$$CH_3AsH_2 + H_2S \longrightarrow CH_3AsS + 2H_2;$$

while alkyl iodides in sealed tubes filled with carbon dioxide at 100–150° for 6-8 hours, yield arsonium compounds:

$$CH_3AsH_2 + 3RI \longrightarrow CH_3.R_3AsI + 2HI.$$

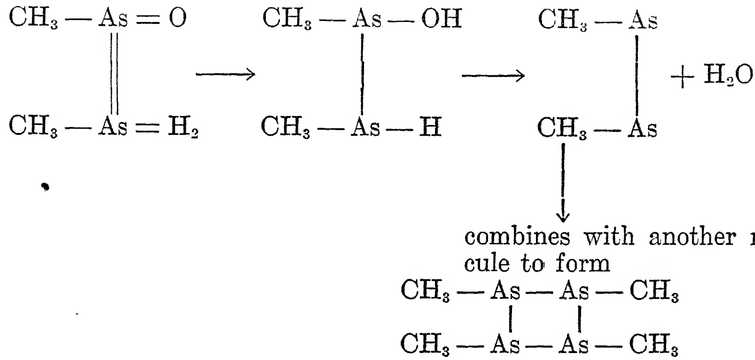
When heated in a sealed tube with carbon dioxide for 3 hours at 310°, methylarsine decomposes into methane, free arsenic and hydrogen:

$$2CH_3AsH_2 \longrightarrow 2CH_4 + 2As + H_2.$$

Methylarsineoxide reacts with methylarsine forming a polymer of arsenomethane:

$$2CH_3AsO + 2CH_3AsH_2 \longrightarrow (CH_3As)_4 + 2H_2O.$$

The phases of the reaction may be represented thus:



Ethylarsine is prepared like the preceding compound from magnesium ethylarsonate, employing a freezing-mixture of salt and ice instead of solid carbon dioxide.[153] If the alcohol is omitted in the above reduction, the product is arsenoethane.

Ethylarsine is a virulent liquid, of an extremely disagreeable, penetrating odor, b. p. 36°, d. 1.217/22°; very slightly soluble in water, and slowly oxidizing in air, forming light-yellow products. With dry oxygen it forms ethylarsineoxide; with concentrated nitric acid it yields ethylarsonic, acetic and arsenic acids, while with silver nitrate, metallic silver is precipitated. Upon passing the arsine through concentrated sulfuric acid and allowing the liquid to stand for a number of days, beautiful white, compact crystals separate which are difficult to obtain free from sulfuric acid. It is probably a salt of the composition $(C_2H_5AsH_2)_2 . H_2SO_4$. With iodine or bromine in a sealed tube containing ether the arsine reacts to form ethyldiiodo- and dibromoarsine respectively; with sulfur in a sealed tube filled with carbon dioxide ethylarsinesulfide is obtained:

$$C_2H_5AsH_2 + S_2 \longrightarrow C_2H_5AsS + H_2S;$$

with mercuric chloride or -iodide, or with stannic chloride the dihalogenated arsine results, while with phosphorus trichloride the products are the dichloroarsine and an unidentified compound. When equimolar quantities of arsenic trichloride and ethylarsine are brought together in a sealed tube containing ether, a polymer $(C_2H_5As)_x$, metallic arsenic, and ethyldichloroarsine are produced:

$$8C_2H_5AsH_2 + 8AsCl_3 \longrightarrow (C_2H_5As)_4 + 4C_2H_5AsCl_2 + 16HCl + 8As.$$

Antimony trichloride reacts similarly, forming a reddish-brown, amorphous solid which slowly turns jet black, and when dried inflames spontaneously. On heating the arsine in a sealed tube at 235° for three hours it decomposes into ethane and triethylarsine:

$$2C_2H_5AsH_2 \longrightarrow 2C_2H_6 + 2As + H_2$$
$$3C_2H_5AsH_2 \longrightarrow (C_2H_5)_3As + 2As + H_2;$$

but it is unaffected by heating with water in a sealed tube at 180° for six hours, or with concentrated hydrochloric acid at 70° for two hours. With alkyl iodides in sealed tubes at 70° it forms arsonium iodides.

n-Propylarsine, prepared by reducing the corresponding arsonic acid, is a volatile liquid.[154]

2. *Alkyl Dihalogenated Arsines*, $RAsX_2$ ($X =$ halogen atom). Within recent years this class of arsenicals has been the subject of considerable investigation, with the result that during the World War, methyl- and ethyldichloroarsines were employed on account of their extremely irritating action upon the mucous membranes of the eyes and nose, and other deleterious effects upon the human body. They were produced on a large scale from the readily available arsenic trioxide, which was first transformed into sodium arsenite, and then converted into either disodium methylarsonate, $CH_3AsO_3Na_2$, by means of dimethyl sulfate, or into the corresponding ethyl derivative with ethyl chloride. By reduction with sulfur dioxide the above arsonates yielded the respective alkyl arsineoxides, which with hydrochloric acid gas gave the desired dihalogenated arsines.[155, 156] The reactions involved are as follows:

$$\begin{cases} Na_3AsO_3 + (CH_3)_2SO_4 \longrightarrow CH_3AsO_3Na_2 + NaCH_3SO_4. \\ Na_3AsO_3 + C_2H_5Cl \longrightarrow C_2H_5AsO_3Na_2 + NaCl. \end{cases}$$
$$RAsO_3Na_2 + 2HCl + SO_2 \longrightarrow RAsO + H_2SO_4 + 2NaCl.$$
$$RAsO + 2HCl \longrightarrow RAsCl_2 + H_2O.$$

These compounds may also be obtained:

1. From primary alkyl arsineoxides and haloid acids as shown above.
2. By the action of dry halogens on primary arsines:

$$\begin{cases} RAsH_2 + X_2 \longrightarrow RAsHX.HX \longrightarrow RAsHX + HX. \\ RAsHX + X_2 \longrightarrow RAsX_2.HX \longrightarrow RAsX_2 + HX. \end{cases}$$

3. From primary alkyl arsonic acids and phosphorus trichloride:

$$RAsO(OH)_2 + PCl_3 \longrightarrow RAsCl_2 + HPO_3 + HCl.$$

4. As a result of the interaction of arsenic trichloride and mercury dialkyls:

$$2AsCl_3 + HgR_2 \longrightarrow 2RAsCl_2 + HgCl_2.$$

5. Upon distilling dialkylarsine trihalides:

$$R_2AsX_3 \longrightarrow RAsX_2 + RX.$$

6. By condensing arsenic trihalides with alkyl halides by means of sodium:

$$RCl + AsCl_3 + 2Na \longrightarrow RAsCl_2 + 2NaCl.$$

The primary aliphatic dihalogenated arsines are colorless liquids generally soluble in alcohol or ether, but decomposed by water. The exceptions to the latter are methyl- and ethyldichloroarsines and methyldiiodoarsine which are slightly soluble.

Methyldichloroarsine, CH_3AsCl_2, is prepared commercially by dissolving arsenic trioxide in caustic soda, converting the resulting trisodium arsenite into disodium methylarsonate with dimethyl sulfate at 85°, and reducing to methylarsineoxide by means of sulfur dioxide. As a result of the action of sulfur dioxide upon the excess of sodium hydroxide, there is also formed sodium bisulfite which is decomposed at the end of the reduction by adding sulfuric acid. Hydrogen chloride is now passed into the mixture to convert the arsineoxide into the corresponding dichloro compound, the introduction of the gas being continued until an excess of about 20 per cent is obtained, thereby producing a constant boiling mixture which distills without decomposition, and also tends to prevent the reconversion of any dichloroarsine to the arsineoxide. Toward the end of the introduction of hydrogen chloride the temperature must be kept above 85° to prevent the formation of arsenic trichloride. Finally, upon distilling the liquid, the distillate separates into two layers, the lower containing the methyldichloroarsine and the upper, the constant boiling hydrochloric acid, from which any dissolved dichloroarsine is salted out by the addition of a saturated solution of calcium chloride. The entire yield of chloroarsine is finally freed from water, methyl alcohol and hydrochloric acid by fractional distillation, collecting the portion coming over between 129° and 132°.[155]

The same product is formed when cacodyl trichloride decomposes at 40–50° according to the equation:

$$(CH_3)_2AsCl_3 \longrightarrow CH_3AsCl_2 + CH_3Cl;$$ [157]

by treating dimethylarsine with an excess of dry chlorine;[158] by carefully introducing methylarsonic acid into an excess of well-cooled phosphorus trichloride and fractionating;[159] or by warming together cacodylic and hydrochloric acids.[160]

Methyldichloroarsine is a colorless, non-fuming liquid boiling at 133°, and is readily hydrolyzed by water.[1594] Its vapors have a terribly irritating effect upon the mucous membranes, and when inhaled produce swelling of the eyes, nose and face and a peculiar gnawing pain extending into the throat. It absorbs chlorine at —10° forming methylarsinetetrachloride. Magnesium does not act upon it in anhydrous ether, but

in the presence of water there is a violent reaction with the formation of methylarsine, hydrogen, methane and a precipitate of $(CH_3As)_x$. With zinc a similar reaction occurs.[161]

Methyldiiodoarsine, CH_3AsI_2.—Prepared by the action of hydriodic acid upon an alcoholic solution of methylarsineoxide;[162] by reducing methylarsinetetraiodide with sulfur dioxide;[163] or by treating methylarsonic acid with sulfur dioxide in the presence of hydrochloric and hydriodic acids.[164] In the last method it is not necessary to actually isolate the arsonic acid, as the above diiodoarsine results upon allowing methyl iodide to react with sodium arsenite in aqueous alcoholic solution for 20 hours, distilling off the solvent, acidifying the residual solution, and saturating with sulfur dioxide.[165]

It crystallizes from alcohol in elongated, yellow, lustrous needles, m. p. 25°, readily soluble in alcohol, ether or carbon bisulfide, sparingly in water, and volatilizing unchanged above 200°.

Ethyldichloroarsine results from the interaction of mercury diethyl and arsenic trichloride at low temperature.[166] It may also be obtained by permitting ethyl iodide and potassium arsenite to react in alcoholic solution according to the method of Dehn, with the formation of ethylarsonic acid. The alcohol and any ethyl ether formed are distilled off on a water-bath, the remaining mixture exactly neutralized with sulfuric acid, and then treated with dimethyl sulfate at the water-bath temperature to eliminate iodine. To the residue one volume of hydrochloric acid is added, the whole filtered, and the filtrate saturated with sulfur dioxide, when ethyldichloroarsine separates as a yellow oily liquid, which is purified by rectification in vacuo.[167] A third method consists in warming ethyldiiodoarsine with calcium chloride and anhydrous sodium carbonate on a water-bath for two hours, and treating the resulting arsineoxide with hydrochloric acid.[168] Commercially the compound is prepared from arsenic trioxide.[156] This is converted into sodium arsenite with concentrated caustic soda solution and stirred with ethyl chloride for 12 to 16 hours under a pressure of 10 to 15 atmospheres. The excess of ethyl chloride and the alcohol formed during the reaction are distilled off, and the residue dissolved in water, neutralized with sulfuric acid and saturated with sulfur dioxide. The mixture is then heated to 70°, and the ethylarsineoxide, which separates out as a heavy oil, is mixed with hydrochloric acid and saturated with hydrogen chloride at a temperature not above 95°.

Ethyldichloroarsine is a colorless liquid with a faint fruity odor, b. p. 156° (LaCoste), 145–150° (Steinkopf), very soluble in water, and miscible with alcohol, ether or benzene in all proportions. It has an extremely irritating effect upon the mucous membranes of the eyes and nose, leaves painful blisters upon the skin, and when inhaled causes

difficulty in breathing, faintness and prolonged paralysis of the extremities.

Ethyldibromoarsine is obtained together with an insoluble, red-brown amorphous solid by the interaction of equimolecular quantities of ethylarsine and bromine in ethereal solution. It exists as an oil boiling at 192° and combining additively with platinic chloride to form a yellowish-white crystalline compound, $C_2H_5AsBr_2.PtCl_4$.[169]

Ethyldiiodoarsine.—Prepared from equimolar quantities of ethylarsine and iodine in a sealed tube containing ether,[169] or from diethylarsinetriiodide by splitting off ethyl iodide.[170] More recently it has been made by reducing ethylarsonic acid with sulfur dioxide as in the case of the corresponding methyl derivative;[165, 168] also by gradually adding ethyldichloroarsine (26 g.) to a solution of sodium iodide (45 g.) in dry acetone (300 c.c.), allowing to react for several hours, distilling off the acetone from the filtrate and extracting the residue with ether. From the latter the diiodoarsine is obtained by removing the solvent, and distilling the remaining liquid under diminished pressure.[171]

The compound is a liquid, b. p. 122.7°/11 mm.; with pyridine and quinoline it forms crystalline compounds soluble in excess of the reagent and reprecipitated by ether.

n-Butyldichloroarsine, $C_4H_9AsCl_2$, is produced by dissolving n-butylarsonic acid (150 g.) in concentrated hydrochloric acid (300 c.c.), adding a few crystals of potassium iodide as a catalyst and saturating with sulfur dioxide, when the crude dichloroarsine separates. After purifying by fractionation under diminished pressure, the pure compound is obtained as a colorless oil, b. p. 192–4°.[172]

Isoamyldichloroarsine, $C_5H_{11}AsCl_2$.—A chloroform solution of phosphorus trichloride is allowed to drop into a similar solution of isoamylarsonic acid, and the whole refluxed for one-half hour on a water-bath. The liquid is then filtered while hot, the filtrate distilled on a water-bath until nothing further comes over, and the residue fractionated in vacuo, the product consisting of a colorless liquid, b. p. 88.5–91.5°/15 mm. It has the characteristic odor of amyl compounds, irritates the nasal mucous membrane, and is decomposed by water in which it is insoluble.[173]

Ethoxydichloroarsine, $(C_2H_5O)AsCl_2$, prepared from equimolar amounts of sodium ethoxide and arsenic trichloride, is a colorless, fuming liquid, b. p. 145-6°/751 mm. When poured into cold water it decomposes with the separation of arsenic trioxide.[174]

β-Chlorovinyldichloroarsine, $CHCl = CH.AsCl_2$, is obtained together with di(β-chlorovinyl) chloroarsine and tri(β-chlorovinyl) arsine upon

introducing dry acetylene into a cooled mixture of anhydrous arsenic- and aluminium trichlorides, allowing the whole to react for six hours, decomposing with ice-cold hydrochloric acid, and fractionating the resulting oil in a current of hydrogen chloride. It is a colorless or faintly yellow liquid, b. p. 93°/26 mm., 96°/30 mm.; insoluble in water or dilute acids, but soluble in all common organic solvents. Cold, dilute alkali hydroxides cause a vigorous reaction, acetylene being evolved with brisk effervescence. It rapidly absorbs halogens, forming a variety of products. Thus, with bromine in carbon tetrachloride solution it yields a bromo compound, consisting of leaflets melting at 122°. The dichloroarsine is a very marked vesicant and a powerful respiratory irritant.[175]

3. *Alkyl Arsineoxides*, RAsO.—These may be regarded as ortho arsenious acid, $As\begin{cases}OH\\OH\\OH\end{cases}$, with one hydroxyl replaced by an alkyl group, $As\begin{cases}R\\OH\\OH\end{cases}$. The latter, however, do not exist as free acids, since they immediately lose one molecule of water forming alkyl arsineoxides which are devoid of acid properties. On the contrary, they exhibit basic properties, reacting with haloid acids to form alkyl dihalogenated arsines and water as shown in the previous chapter. The methods of preparation are:

1. The action of alkali hydroxides or carbonates upon primary alkyl dihalogenated arsines:

$$RAsCl_2 + 2KOH \longrightarrow RAsO + 2KCl + H_2O$$
$$RAsCl_2 + K_2CO_3 \longrightarrow RAsO + 2KCl + CO_2.$$

2. Reduction of primary arsonic acids by means of sulfur dioxide:

$$RAsO(OH)_2 + SO_2 \longrightarrow RAsO + H_2SO_4.$$

3. Alkylation of sodium arsenite and subsequent reduction with sulfur dioxide as already described under methyl and ethyl dichloroarsines.

4. The oxidation of primary arsines by means of atmospheric oxygen:

$$RAsH_2 + O \longrightarrow RAsO + H_2O.$$

Methylarsineoxide, CH_3AsO.—Prepared from methyldichloroarsine by treating with potassium hydroxide or carbonate solution;[176] by reducing disodium methylarsonate with sulfur dioxide;[177] from methyldiiodoarsine and sodium carbonate in benzene solution;[159] or from sodium arsenite by first methylating with dimethyl sulfate and then reducing

with sulfur dioxide as described under the preparation of methyldichloroarsine.[155]

It consists of colorless crystals with an odor of asafetida, m. p. 95°; soluble in water, alcohol, ether, carbon bisulfide or hot benzene, and slightly volatile in steam. Distilled with potassium hydroxide, it decomposes into cacodyl oxide and arsenic trioxide:

$$4CH_3AsO \longrightarrow As_2O_3 + [(CH_3)_2As]_2O.$$

With hydrogen sulfide it forms the corresponding arsinesulfide.

Ethylarsineoxide is obtained from ethyldichloroarsine and potassium carbonate in benzene medium.[178] For large scale production it is prepared from arsenic trioxide as described under ethyldichloroarsine, by being first converted into sodium arsenite, then ethylated by means of ethyl chloride under pressure, and the resulting product reduced to the arsineoxide with sulfur dioxide.[156] It is a colorless oil, b. p. 158°/10 mm., which oxidizes rapidly in air, and is readily soluble in ether, benzene or acetone.

4. *Alkyl Arsinesulfides,* RAsS.—Compounds of this type may be regarded as arsineoxides with the oxygen replaced by sulfur. This is borne out by the action of hydrogen sulfide upon arsineoxides, which proceeds according to the equation:

$$RAsO + H_2S \longrightarrow RAsS + H_2O.$$

Other methods of preparation depend upon:

1. The action of hydrogen sulfide upon primary dihalogenated arsines:

$$RAsX_2 + H_2S \longrightarrow RAsS + 2HX.$$

2. The interaction of sulfur and primary aliphatic arsines:

$$RAsH_2 + S_2 \longrightarrow RAsS + H_2S.$$

Methylarsinesulfide, CH_3AsS.—Prepared from methyldichloroarsine or methylarsineoxide and hydrogen sulfide.[179] It crystallizes as colorless leaflets or small prisms, m. p. 110°; has an odor resembling asafetida, is readily soluble in carbon bisulfide, less so in alcohol or ether and insoluble in water. It is stable in air but is decomposed on heating, yielding arsenic trisulfide.

Ethylarsinesulfide.—When one mole of ethylarsine and two atomic equivalents of sulfur are brought together in a sealed tube filled with carbon dioxide, the sulfur rapidly dissolves and a viscid, colorless liquid results:

$$C_2H_5AsH_2 + S_2 \longrightarrow C_2H_5AsS + H_2S.^{180}$$

β-Chlorovinylarsinesulfide, $CHCl = CH.AsS$, is formed on treating a carbon tetrachloride solution of the corresponding dichloroarsine with hydrogen sulfide. The product obtained thus far is impure, consisting of a pale yellow liquid having a garlicky odor, and solidifying to a hard resinous mass on cooling.[181]

5. *Aliphatic Arseno Compounds.—Arsenomethane,* $CH_3As = AsCH_3$, obtained by reducing methylarsonic acid with hypophosphorous acid in the presence of sulfuric acid at water-bath temperature, is a heavy yellow oil with a strong garlicky odor, b. p. 190°/13 mm.; slightly soluble in alcohol or benzene, more readily in hot glacial acetic acid, but immiscible with water. It oxidizes slowly in air, more rapidly in benzene solution; yields methyl dihalogenated arsines with halogens, while with methyl iodide at 100° it forms tetramethylarsonium iodide and methyldiiodoarsine, thereby resembling arsenobenzene, which under similar circumstances yields tetraphenylarsonium iodide and phenyldiiodoarsine: [182]

$$CH_3As = AsCH_3 + 3CH_3I \longrightarrow CH_3AsI_2 + (CH_3)_4AsI.$$

A red polymer, $\begin{array}{c} CH_3As - AsCH_3 \\ | \quad\quad\quad | \\ CH_3As - AsCH_3 \end{array}$, is obtained during the reduction of methylarsonic acid to the arsine when alcohol is omitted. It is also formed by the action of methylarsine upon the corresponding arsineoxide:

$$2CH_3AsH_2 + 2CH_3AsO \longrightarrow (CH_3)_4As + 2H_2O.^{183}$$

Its addition product with arsenic trioxide, $(CH_3As)_4.As_2O_3$, "Erytrarsin" is a red substance isolated by Bunsen from among the decomposition products of cacodyl or impure cacodyl oxide and -chloride.[184]

Another polymer, $(CH_3As)_x$, is a dark-brown, insoluble powder obtained by reducing methylarsonic acid with hypophosphorous acid in the presence of hydrochloric instead of sulfuric acid.[185] It is also produced by heating dimethylarsine in a sealed tube at 335°.[186] When distilled in hydrogen it decomposes quantitatively into trimethylarsine and arsenic, resembling arsenobenzene which, on heating, quantitatively yields triphenylarsine and free arsenic:

$$3CH_3As \longrightarrow (CH_3)_3As + As_2.$$

B. Secondary Derivatives.

1. *Dialkyl Arsines,* R_2AsH.—Although the first member of this series, dimethylarsine, was prepared by Palmer,[36] it remained for Dehn [187] to extensively investigate and develop the compounds included in this chapter. Like the primary aliphatic arsines, the secondary compounds possess but feebly basic properties. The one exception is the strongly basic dimethylarsine, which combines additively with sulfuric acid, yield-

ing a well-defined crystalline salt, $[(CH_3)_2AsH]_2.H_2SO_4$, decomposing slowly in moist air, but very rapidly in water. It also forms very unstable salts of the type, $(CH_3)_2AsH.HX$, with haloid acids, while with platinic chloride it forms double salts analogous to those of the corresponding amine.

The dialkylated arsines are more reactive than the primary compounds. Thus, dimethylarsine reacts very readily with such inorganic substances as oxygen, sulfur, halogens, haloid acids, halides of heavy metals, oxides, sulfides, oxygenated acids and their salts. As to the organic compounds, its reactions with alkyl halides and those substances upon which it acts as a reducing agent are the most characteristic.

With halogens, compounds of the type $R_2AsH.X_2$, R_2AsX and R_2AsX_3 are formed:

$$R_2AsH + X_2 \longrightarrow R_2AsH.X_2 \longrightarrow R_2AsX + HX \xrightarrow{X_2} R_2AsX_3;$$

with haloid acids, salts of the type $R_2AsH.HX$ are first produced, but these very quickly decompose into dialkyl halogenated arsines and hydrogen:

$$R_2AsH + HX \longrightarrow R_2AsH.HX \longrightarrow R_2AsX + H_2.$$

Heavy metal halides form dialkylhalogenated arsines:

$$R_2AsH + MX_2 \longrightarrow R_2AsX + M + HX \quad (M = \text{metal});$$

while sulfur yields either mono- or disulfides depending upon the amount employed:

$$2R_2AsH + S_2 \longrightarrow (R_2As)_2S + H_2S$$
$$2R_2AsH + S_3 \longrightarrow (R_2As)_2S_2 + H_2S.$$

The affinity of aliphatic arsines for oxygen increases with the number of alkyl groups present. Thus, hydrogen arsenide does not react with that element at ordinary temperatures; the primary arsines readily react but not with the spontaneous inflammability characteristic of the secondary and tertiary arsines. The dialkyl arsines may be oxidized to compounds of the type $R_2As.AsR_2$, $R_2As.O.AsR_2$ or $R_2AsO.OH$, depending upon the oxidizing agent employed. With alkyl halides, especially the iodides, addition products of the type $R_2AsH.R'I$, and $R_2R'_2AsI$ are formed:

$$\begin{cases} R_2AsH + R'I \longrightarrow R_2AsH.R'I \longrightarrow R_2R'As + HI \\ R_2R'As + R'I \longrightarrow R_2R'_2AsI. \end{cases}$$

The secondary aliphatic arsines may be prepared:

1. By reducing the corresponding oxides or arsinic acids with amalgamated zinc dust and hydrochloric acid:

$$(R_2As)_2O + 2H_2 \longrightarrow 2R_2AsH + H_2O$$
$$R_2AsO.OH + 2H_2 \longrightarrow R_2AsH + 2H_2O.$$

2. From dialkyl halogenated arsines by reduction with platinized zinc and hydrochloric acid in alcoholic solution:

$$R_2AsX + H_2 \longrightarrow R_2AsH + HX.$$

3. By the dry distillation of tetraalkylarsonium compounds. In the preparation of these compounds the access of either air or moisture must be carefully guarded against.

Dimethylarsine, $(CH_3)_2AsH$, was first prepared by reducing cacodyl chloride with nascent hydrogen. Platinized zinc is covered with alcohol, enough hydrochloric acid added to generate a rapid stream of hydrogen and a mixture of cacodyl chloride, hydrochloric acid and alcohol is gradually introduced. The resulting gaseous mixture of hydrogen and dimethylarsine is washed by passing through two U-tubes containing water, then dried by passing through a third tube containing granular calcium chloride, and finally collected in a receiver immersed in a mixture of ice and salt, the dimethylarsine condensing, while the hydrogen and other volatile products remain unaffected and are subsequently collected over water. If the cacodyl chloride is introduced too rapidly, or if an insufficient amount of hydrochloric acid is present, the main product obtained is cacodyl which, because of its high boiling point, either remains behind in the generator or is retained in the U-tubes containing the water.[36]

Since the preparation of cacodyl chloride from cacodyl oxide by treatment with mercuric chloride and hydrochloric acid[188] is attended with considerable inconvenience, an easier method of securing the above arsine was developed by Dehn, which depended upon the direct reduction of the crude "arsenical liquor of Cadet."[189] The yields thus obtained were not very satisfactory, due to the small amounts of cacodyl oxide present in the above "liquor." By employing cacodyl oxide alone, however, the product was obtained in good yields. Zinc dust, cacodyl oxide and alcohol are introduced into a round-bottomed flask and concentrated hydrochloric acid slowly admitted. The generator is joined in series with a water wash-bottle, a U-tube filled with soda-lime, a bulb condenser for dimethylarsine surrounded with ice and salt, and two wash-bottles—one containing sulfuric and the other nitric acid. The connections throughout must be of glass and cork, as rubber is easily attacked by the arsine. When air is present in the apparatus a red substance always appears; this contains a polymeride of arsenomethane and is identical with Bunsen's "Erytrarsin." In the above procedure reduction takes place in two stages:

$$\begin{cases} [(CH_3)_2As]_2O + H_2 \longrightarrow (CH_3)_2As.As(CH_3)_2 + H_2O \\ (CH_3)_2As.As(CH_3)_2 + H_2 \longrightarrow 2(CH_3)_2AsH. \end{cases}$$

The product, which can only be preserved in sealed tubes, is a colorless mobile liquid, b. p. 35.6°/747 mm., 55°/1.74 atmos.; d. 1.213/29°. It has a characteristic cacodylic odor, and is miscible in all proportions with alcohol, ether, chloroform, carbon bisulfide or benzene. It is very volatile, inflaming spontaneously in the air even at 0–10° and burning with a blue-white arsenical flame. When exposed to direct sunlight for two weeks in an almost completely evacuated sealed tube, then heated for one hour at 192° and for two more hours at 242°, no evident change is observed. But upon continued heating for another hour at 335°, the inner surface of the tube becomes covered with a beautiful, lustrous, black, metallic mirror of the polymer $(CH_3As)_x$, with the simultaneous liberation of a gas which burns with a blue flame. The reaction involved is either:

$$X(CH_3)_2AsH \longrightarrow (CH_3As)_x + XCH_4$$
$$\text{or } X(CH_3)_2AsH \longrightarrow (CH_3As)_x + \frac{X}{2}C_2H_6 + \frac{X}{2}H_2.$$

Dimethylarsine acts as a reducing agent—it precipitates metallic silver from aqueous silver nitrate; reduces the oxides of nitrogen to either nitrous oxide or nitrogen, while it is itself variously oxidized, cacodylic acid being the product generally obtained:

$$2(CH_3)_2AsH + 4NO \longrightarrow [(CH_3)_2As]_2O + H_2O + 2N_2O$$
$$2(CH_3)_2AsH + N_2O_4 \longrightarrow 2(CH_3)_2AsO.OH + N_2$$
$$8(CH_3)_2AsH + N_2O_4 \longrightarrow 4[(CH_3)_2As]_2 + N_2 + 4H_2O$$
$$(CH_3)_2AsH + 2HNO_2 \longrightarrow (CH_3)_2AsO.OH + N_2O + H_2O.$$

With nitric acid it yields cacodylic acid:

$$(CH_3)_2AsH + 4HNO_3 \longrightarrow (CH_3)_2AsO.OH + 4NO_2 + 2H_2O.$$
$$5(CH_3)_2AsH + 4HNO_3 \longrightarrow 5(CH_3)_2AsO.OH + 2N_2 + 2H_2O;$$

with small amounts of chromic acid, cacodyl, but with an excess of the reagent cacodylic acid results:

$$6(CH_3)_2AsH + 2H_2CrO_4 \longrightarrow 3[(CH_3)_2As]_2 + 2Cr(OH)_3 + 2H_2O$$
$$3(CH_3)_2AsH + 4H_2CrO_4 + 2H_2O \longrightarrow 3(CH_3)_2AsO.OH + 4Cr(OH)_3.$$

Potassium chromate is reduced to $CrO_2.H_2O$; lead peroxide or mercuric chloride to the metal; ferric chloride to the ferrous salt; potassium ferricyanide in alkaline solution to the ferrocyanide, and molybdic acid to the hydrated molybdenum dioxide:

$$\begin{cases} 4(CH_3)_2AsH + 5PbO_2 \longrightarrow 2[(CH_3)_2AsO_2]_2Pb + 3Pb + 2H_2O \\ 4(CH_3)_2AsH + PbO_2 \longrightarrow 2[(CH_3)_2As]_2 + Pb + 2H_2O \end{cases}$$
$$(CH_3)_2AsH + HgCl_2 \longrightarrow (CH_3)_2AsCl + Hg + HCl$$
$$(CH_3)_2AsH + 2FeCl_3 \longrightarrow (CH_3)_2AsCl + 2FeCl_2 + HCl$$

$$\begin{cases} (CH_3)_2AsH + 4K_3Fe(CN)_6 + 5KOH \longrightarrow 4K_4Fe(CN)_6 + \\ \quad (CH_3)_2AsO.OK + 3H_2O \\ 4(CH_3)_2AsH + 4K_3Fe(CN)_6 + 4KOH \longrightarrow 2[(CH_3)_2As]_2 + 4H_2O + \\ \quad K_4Fe(CN)_6; \end{cases}$$

$$2H_2MoO_4 + (CH_3)_2AsH \longrightarrow (CH_3)_2AsO.OH + 2MoO_2H_2O.$$

With sulfur dioxide the following reactions occur:

$$\begin{cases} 7(CH_3)_2AsH + 4SO_2 \longrightarrow 2CH_3)_3AsS + 2CH_3AsS + 3(CH_3)_2AsO.OH \\ \quad + 2H_2O \\ 7(CH_3)_2AsH + 4SO_2 \longrightarrow 2[(CH_3)_2As]_2S_2 + 3(CH_3)_2AsO.OH \\ \quad + 2H_2O; \end{cases}$$

with sulfur monochloride dimethylchloroarsine is obtained:

$$2(CH_3)_2AsH + S_2Cl_2 \longrightarrow 2(CH_3)_2AsCl + S + H_2S.$$

Stannic chloride reacts with dimethylarsine forming dimethylarsine-chlorostannide, $(CH_3)_2As.SnCl_3$, which upon sublimation yields beautiful, large, colorless, deliquescent needles, having a very disagreeable, penetrating odor, and readily soluble in ether or carbon bisulfide, though less so in chloroform.

With phosphorus-, arsenic- or antimony trichloride, dimethylarsine forms cacodyl chlorine, hydrochloric acid and other unidentified products, while heating with arsenic trioxide in a sealed tube filled with carbon dioxide at 100° for five hours and allowing to stand for two years yields a dark brown solid, largely $(CH_3As)_4$:

$$2CH_3AsH + As_2O_3 \longrightarrow (CH_3As)_4 + H_2O + O_2.$$ [190]

With sulfur, dimethylarsine forms either the mono or disulfide depending upon the quantity of sulfur; with dry chlorine at ordinary temperature the final product is mainly methyldichloroarsine; with bromine, $(CH_3)_2AsBr.HBr$; and with iodine, $(CH_3)_2AsI.HI$. Bromine in the presence of water, however, produces cacodyl bromide and a dark-brown, amorphous solid which is probably identical with Bunsen's "Erytrarsin," while aqueous iodine yields cacodylic acid:

$$(CH_3)_2AsH + 4I + 2H_2O \longrightarrow (CH_3)_2AsO.OH + 4HI.$$

With pure, dry hydrobromic acid, the product is a hydrobromide, $(CH_3)_2AsH.HBr$, which decomposes at —10 to 20° into dimethylbromoarsine and hydrogen. The latter two products are also obtained directly on heating dimethylarsine with a slight excess of aqueous hydrobromic acid in a sealed tube at 125° for 24 hours. Dry hydriodic acid produces a white crystalline mass which soon becomes effervescent and changes to cacodyl iodide.

With an excess of platinic chloride the arsine forms a double salt, $(CH_3)_2AsH.H_2PtCl_6$, which decomposes with liberation of hydrogen and hydrochloric acid, yielding the compound $(CH_3)_2AsCl.PtCl_4$. but with an

excess of the arsine the product is $[(CH_3)_2AsH]_2H_2PtCl_6$. These compounds have not been obtained in pure form. Auric chloride in aqueous solution is reduced to the metallic condition, the dimethylarsine being oxidized to a mixture of cacodyl, cacodyl chloride and cacodylic acid.

When equimolar quantities of dimethylarsine and ethyl chlorocarbonate are brought together in a sealed tube filled with carbon dioxide no reaction is evident, but upon opening the tube combustible vapors are evolved. The residual oil is cacodyl chloride and is produced according to the reaction:

$$(CH_3)_2AsH + ClOOCC_2H_5 \longrightarrow (CH_3)_2AsCl + HOOCC_2H_5.$$ [191]

Oxygen acts upon dimethylarsine according to the following equations:

1. $6(CH_3)_2AsH + 3O_2 \longrightarrow 2(CH_3As)_4.As_2O_3 + 2C_2H_6 + 3H_2O.$
2. $4(CH_3)_2AsH + O_2 \longrightarrow 4(CH_3As)_x + 2C_2H_6 + 2H_2O.$
3. $4(CH_3)_2AsH + O_2 \longrightarrow As_4 + 4C_2H_6 + 2H_2O.$
4. $2(CH_3)_2AsH + 9O_2 \longrightarrow As_2O_3 + 4CO_2 + 7H_2O.$
5. $4(CH_3)_2AsH + O_2 \longrightarrow 2[(CH_3)_2As]_2 + 2H_2O.$
6. $2(CH_3)_2AsH + O_2 \longrightarrow [(CH_3)_2As]_2O + H_2O.$
7. $(CH_3)_2AsH + O_2 \longrightarrow (CH_3)_2AsO.OH.$

The arsine reacts with dimethylchloroarsine, yielding cacodyl:

$$(CH_3)_2AsH + (CH_3)_2AsCl \longrightarrow (CH_3)_2As.As(CH_3)_2 + HCl;$$

while with dibromosuccinic acid, cacodyl bromide is obtained:

$$2(CH_3)_2AsH + C_2H_2Br_2(COOH)_2 \longrightarrow 2(CH_3)_2AsBr + C_2H_4(COOH)_2.$$

Upon mixing dimethylarsine with concentrated sulfuric acid in a sealed tube filled with carbon dioxide, colorless prismatic crystals of the sulfate, $[(CH_3)_2AsH]_2.H_2SO_4$, are produced. This decomposes slowly in air but rapidly in water, regenerating its components.

Diethylarsine has not been definitely prepared. According to Gosio [1] various species of moulds, such as mucor mucedo, aspergillus glaucus and especially penicillium brevicaule, act upon arsenic compounds generating a very poisonous gas containing arsenic and capable of killing a mouse in a few seconds. The same phenomenon was noted by other observers,[3] who had not identified the gaseous product. Gosio also concluded that poisoning cases occurring in rooms furnished with wall papers or carpets containing arsenical coloring matters were due to the above phenomenon, although the composition of the toxic compound remained unknown. O. Emmerling,[2] upon repeating Gosio's experiments was unable to confirm the latter's conclusions. He therefore advanced the theory that the cases of arsenical poisoning previously mentioned are not due to any volatile arsenical but to the inhalation of dust particles of the arsenical compound present in the wall papers or carpets.

Finally, Biginelli [4] thoroughly investigated the gas noted by Gosio, and found that upon passing it into a hydrochloric acid solution of mercuric chloride, there separate colorless, tabular, triclinic crystals of the composition $[(C_2H_5)_2AsH.2HgCl_2]_2$. It sinters at 239–40°, decomposes at 255–6°, and dissolves in boiling water, from which, upon cooling, a small quantity of a substance decomposing at 250–1° is obtained together with the oxide, $O\left\langle\begin{array}{l} AsH(C_2H_5)_2 \\ \vert \\ AsH(C_2H_5)_2 \end{array}\right..4HgCl_2$. The latter separates in shining scales sintering at 270° but is not completely fused at 290°. When treated successively with concentrated aqueous caustic potash and an ethereal solution of iodine it yields hygroscopic, straw-yellow needles of $O\left\langle\begin{array}{l} AsH(C_2H_5)_2.I \\ \vert \\ AsH(C_2H_5)_2.I \end{array}\right.$, m. p. 102°, which with silver sulfate forms the sulfate $(C_4H_{11}OAs)_2SO_4$, m. p. 210°; with moist silver oxide, deliquescent needles of the dioxide, $(C_2H_5)_2H.As{<}^{O}_{O}{>}As.H(C_2H_5)_2$; and with potassium permanganate in nitric acid solution, the compound $O[AsH(C_2H_5)_2.OH]_2.KNO_3$ — hygroscopic, acicular prisms melting at 129–31° and exploding at higher temperatures. By passing the arsenical gas evolved by P. brevicaule into mercuric nitrate solution there is precipitated an insoluble, infusible, yellow substance, $(C_2H_5)_2AsH.2HgNO_3$, which is not decomposed by boiling water.

Although he was unable to isolate diethylarsine itself, Biginelli concluded that the formation of the foregoing compounds is sufficient evidence of its production from arsenical compounds contained in wall paper.

Di-n-propylarsine, $(C_3H_7)_2AsH$, is obtained together with other decomposition products in the dry distillation of the so-called "hexapropyldiarsonium hydroxide," but actually tetrapropylarsonium hydroxide, in an atmosphere of hydrogen.[192]

Diisoamylarsine, $(C_5H_{11})_2AsH$, prepared by reducing diisoamylarsinic acid with amalgamated zinc dust and hydrochloric acid in the presence of ether, is a colorless liquid, b. p. 150°/99 mm., having an odor resembling that of isoamyl alcohol. On exposure to air it oxidizes without inflaming, yielding diisoamylarsineoxide and the corresponding arsinic acid.[193] When heated at 240–60° for 3 hours it decomposes according to the following equations:

$$6(C_5H_{11})AsH \longrightarrow 4(C_5H_{11})_3As + 2As + 3H_2$$
$$2(C_5H_{11})AsH \longrightarrow C_5H_{10} + C_5H_{12} + C_{10}H_{22} + 2As$$ [194]

2. *Dialkyl Halogenated- and Cyanoarsines,* R_2AsX.—As we have already seen, the hydrogen of the secondary arsines may be readily replaced with a halogen, by means of a haloid acid:

$$R_2AsH + HX \longrightarrow R_2AsX + H_2,$$

thereby furnishing conclusive evidence as to the chemical constitution of the secondary halogenated arsines. On the other hand, they may be regarded as arsenic trihalides in which two of the halogen atoms have been replaced by alkyl groups. This is well borne out by a general method of synthesis consisting of the interaction of one molecular equivalent of arsenic trihalide with two of an alkyl halide in the presence of two molecules of sodium:

$$2RX + AsX_3 + 2Na_2 \longrightarrow R_2AsX + 4NaX.$$

From a practical standpoint, the most satisfactory method of preparation consists in reducing an arsinic acid with hypophosphorous acid in the presence of the respective haloid acid. This procedure offers a distinct advantage over that in which the haloid acid is permitted to react with secondary arsines, because of the difficulty involved in handling the latter.

The methods employed in the preparation of secondary halogenated aliphatic arsines depend upon:

1. The action of haloid acids upon secondary arsines:

$$R_2AsH + HX \longrightarrow R_2AsH.HX \longrightarrow R_2AsX + H_2.$$

2. Condensation of arsenic trihalides with alkyl halides by means of metallic sodium.

3. Reduction of aliphatic arsinic acids with hypophosphorous acid in the presence of a haloid acid, e. g.:

$$2(CH_3)_2AsO.OH + 3H_3PO_2 + 2HCl \longrightarrow 2R_2AsCl + 3H_3PO_3 + H_2O.$$

4. The action of phosphorus trichloride upon arsinic acids, e. g.:

$$2(CH_3)_2AsO.OH + 2PCl_3 \longrightarrow (CH_3)_2AsCl + POCl_3 + HPO_3$$
$$\text{or } 3(CH_3)_2AsO.OH + 4PCl_3 \longrightarrow 3(CH_3)_2AsCl + 3POCl_3 + H_3PO_3.$$

5. Distillation of secondary arsineoxides with concentrated haloid acids in the presence of mercuric chloride, e. g.:

$$[(CH_3)_2As]_2O + 2HgCl_2 + 2HCl \longrightarrow 2(CH_3)_2AsCl + H_2O + 2HgCl_2.$$

6. The interaction of halogens and aliphatic cacodyls in ethereal solution:

$$(CH_3)_2As - As(CH_3)_2 + X_2 \longrightarrow 2(CH_3)_2AsX.$$

7. The action of alkyl halides upon tetraalkyldiarsines:

$$(CH_3)_2As.As(CH_3)_2 + 2CH_3I \longrightarrow (CH_3)_2AsI + (CH_3)_4AsI.$$

The dialkyl halogenated arsines are virulent, oily liquids with an unbearable odor. They can be readily obtained pure by distilling in vacuo or in an atmosphere of inert gas, are generally insoluble in water, soluble in the usual organic solvents, and oxidize readily on exposure to air. When heated with alkyl halides in a sealed tube, they yield tetra-alkylarsonium halides.

The dialkyl cyanoarsines, R_2AsCN, are extremely poisonous compounds which may be obtained by the action of either hydrocyanic acid or mercuric cyanide solution upon the corresponding arsineoxides. The dimethyl compound is a solid at ordinary temperatures, while the diethyl derivative is a liquid. A particularly interesting method of preparing the latter consists in distilling triethylarsine bromocyanide, $(C_2H_5)_3AsCN.Br$, under reduced pressure, the reaction proceeding according to the following equation:

$$(C_2H_5)_3As.CN.Br \longrightarrow (C_2H_5)_2As.CN + C_2H_5Br.$$

In addition, a dimethylthiocyanoarsine, $(CH_3)_2As.CNS$, has been prepared by the action of sodium thiocyanate upon dimethylchloroarsine, thereby differing from both the primary aliphatic and aromatic dihalogenated arsines, which do not yield the corresponding dithiocyanoarsines with sodium thiocyanate—an indication that arsenic is incapable of combining with two CNS radicals.

Dimethylchloroarsine (Cacodyl chloride), $(CH_3)_2AsCl$.—The earliest method of preparation consisted in mixing "Cadet's crude arsenical liquid" with an excess of concentrated hydrochloric acid and treating with an excess of powdered mercuric chloride, the mixture setting to a thick, crystalline magma. This was rendered liquid by the addition of more hydrochloric acid and distilled. The cacodyl chloride obtained in the distillate was dried with calcium chloride, freed from excess of hydrochloric acid with powdered calcium carbonate and then rectified.[195] A more modern procedure consists in dissolving cacodylic acid in an excess of concentrated hydrochloric acid and reducing with a solution of hypophosphorous acid in the same reagent below 50°. The latter solution is divided into two portions, the second being added after the reaction with the first is completed. Cacodyl chloride separates as a heavy faint-yellow oil which is removed in a separatory funnel, dried with calcium chloride and distilled in an atmosphere of carbon dioxide.[196] According to another method cacodylic acid is gradually introduced into well-cooled phosphorus trichloride, cold, concentrated hydrochloric acid added to decompose the phosphorus oxychloride which forms, and the whole subjected to fractional distillation.[197]

Cacodyl chloride is a colorless, ethereal, non-fuming liquid heavier than water, boiling at 106.5–107°, soluble in alcohol in all proportions, insoluble in water or ether, and cannot be solidified at —45°. It has a very penetrating and stupefying odor, and an intensely irritating action upon the eyes and nose. Oxygen converts it into a well-defined, crystalline oxidation product, but when heated in the air it burns with a pale flame. With chlorine it forms dimethylarsinetrichloride; with alkalis—cacodyl oxide, while with soluble silver salts, silver chloride is precipitated. Zinc and hydrochloric acid reduce it to dimethylarsine. It forms double salts with metallic chlorides. Thus, the platinichloride, $[(CH_3)_2AsCl]_2.PtCl_4$, is a brick-red precipitate soluble in hot water to a colorless solution, from which the compound, $[(CH_3)_2As]_2O.PtCl_2.H_2O$, separates in colorless needles which are dehydrated at 160°, and also react with potassium bromide or iodide, silver nitrate or sulfate yielding respectively $[(CH_3)_2As]_2O.PtBr_2.H_2O$ (colorless), $[(CH_3)_2As]_2O.PtI_2.H_2O$ (yellow), $[(CH_3)_2As]_2O.Pt(NO_3)_2.H_2O$ and $[(CH_3)_2As]_2O.PtSO_4.H_2O$,[198] while with cuprous chloride a white precipitate of the double salt, $[(CH_3)_2AsCl]_2.Cu_2Cl_2$, is formed.[199] On heating a mixture of cacodyl chloride and methyl iodide in a sealed tube for 3 hours at 100°, tetramethylarsonium triiodide, $(CH_3)_4AsI.I_2$, and methyl chloride are obtained.[200]

Dimethylbromoarsine (*Cacodyl bromide*) is prepared either by distilling cacodyl oxide-mercuric chloride with very concentrated hydrobromic acid; [201] from cacodyl and methyl bromide; [202] or from dimethylarsine by heating in a sealed tube with a 45 per cent solution of hydrobromic acid at 125° for 24 hours: [203]

$$(CH_3)_2AsH + HBr \longrightarrow (CH_3)_2AsBr + H_2.$$

The most convenient method, however, consists in reducing a solution of cacodylic acid in hydrobromic acid with hypophosphorous acid as described under the corresponding chloride.[204]

It is a yellow oil, b. p. 128–9° in an atmosphere of carbon dioxide. When heated with methyl iodide in a sealed tube for two hours at 100°, it forms tetramethylarsonium triiodide; with methyl bromide in a sealed tube filled with dry carbon dioxide for three hours in a boiling water bath, trimethylarsine dibromide results, while heating with methylarsonium triiodide under the same conditions for six hours yields the corresponding arsonium iodide together with unchanged triiodide.[205]

The hydrobromide, $(CH_3)_2AsBr.HBr$, is obtained by the interaction of dimethylarsine and an excess of bromine in a sealed tube. It forms white tabular crystals slightly soluble in hot chloroform, less so in carbon bisulfide, and insoluble in ether. It is stable in air, but is slowly decomposed by cold water, more readily upon heating, yielding the bromoarsine and hydrobromic acid.[206]

Dimethyliodoarsine (Cacodyl iodide) has been obtained by distilling cacodyl oxide with concentrated hydriodic acid;[207] in small amounts together with tetramethylarsonium iodide by the interaction of methyl iodide and cacodyl;[202] and from dimethylarsine and hydriodic acid.[208] The following are the modern methods of preparation: 1. An aqueous solution of cacodylic acid and potassium iodide is saturated with sulfur dioxide, 1:1 hydrochloric acid being added from time to time. The cacodyl iodide then separates as a yellow oil, which is dried over calcium chloride and distilled.[209] 2. Methyldiiodoarsine and methyl iodide are permitted to react in alcohol-concentrated aqueous caustic soda solution over night, the solvent distilled off, the residue acidified with hydrochloric acid and saturated with sulfur dioxide.[210] 3. Cacodyl chloride is gradually added to a solution of sodium iodide in dry acetone and the resulting solution permitted to stand for several hours in an atmosphere of carbon dioxide. After filtering and distilling off the acetone from the filtrate, the residue is taken up with ether, the solvent removed from the extract by distillation, and the residue rectified in an atmosphere of carbon dioxide.[211]

Cacodyl iodide is a yellow oil boiling at 154–7°, and solidifying at —35° to pale yellow crystals. It has a penetrating, nauseating odor like the corresponding chloride, is insoluble in water but dissolves readily in alcohol or ether. It does not fume in the air, but on standing for a short time is converted into prismatic crystals, while upon heating it burns with the evolution of iodine vapors. Both sulfuric and nitric acids cause decomposition with liberation of iodine. By heating cacodyl iodide with methyl iodide in a sealed tube for one hour at 100°, tetramethylarsonium triiodide is obtained.

The hydriodide, $(CH_3)_2AsI.HI$, is made from equimolar amounts of dimethylarsine and iodine in a sealed tube at ordinary temperature. It forms large, pale yellow needles, m. p. 175°, soluble in alcohol with decomposition, insoluble in ether or chloroform. Water decomposes it into cacodyl iodide and hydriodic acid.[212]

Dimethylfluoroarsine (Cacodyl fluoride), a colorless liquid with an unbearable, repulsive odor, was first prepared by Bunsen in a manner similar to the corresponding chloride. The product has a corrosive action upon glass and must therefore be preserved in platinum containers. It is insoluble in water but is apparently decomposed by it.[201]

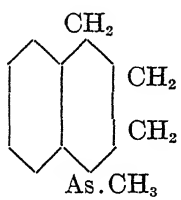
Basic dimethyl halogenated arsines $[(CH_3)_2AsX]_6.[(CH_3)_2As]_2O$.—*Basic dimethylchloroarsine*, formed by a distilling cacodyl oxide with dilute hydrochloric acid, is a liquid, b. p. 109°;[213] the *bromo* compound, similarly prepared, is a yellow fuming liquid,[207] while the yellow, crystalline *iodo* derivative is formed together with cacodyl iodide upon dis-

ling cacodyl oxide with concentrated hydriodic acid.[214] Bayer, how-
er, questions the existence of these compounds.[215]

Diethyliodoarsine, $(C_2H_5)_2AsI$, is obtained upon saturating ar hereal solution of ethyl cacodyl with a similar solution of iodine and aporating in vacuo.[216] It may also be prepared by heating together hyl iodide and metallic arsenic, distilling the resulting red, crystalline bstance, $(C_2H_5)_4AsI.AsI_3$, and collecting the fraction coming over tween 228° and 232°.[217] It is a yellow oil, soluble in ether or alcohol, soluble in water, and decomposed by nitric or sulfuric acid with libera-on of iodine.

Methylethyliodoarsine, $(CH_3)(C_2H_5)AsI$.—An aqueous caustic alka-le solution of ethyldiiodoarsine is refluxed for a few hours with methyl dide, the solution neutralized, freed from alcohol, acidified with hydro-loric acid and finally saturated with sulfur dioxide. The resulting l is collected, dried and distilled under reduced pressure, yielding a llow, oily liquid, b. p. 65°/14 mm. Under ordinary pressure it boils ith slight decomposition, spontaneous ignition occurring occasionally.[218]

Methyl-γ-phenylpropylchloroarsine, $(CH_3)(C_6H_5.C_3H_6)AsCl$.—Phenylpropyldimethylarsine dissolved in carbon tetrachloride, is treated ith a solution of chlorine (1 mole) in the same reagent, the solvent moved by distillation, and the residue heated at 160–80°, when methyl loride, volatile chloroarsines and γ-chloropropylbenzene are evolved. pon distilling the final residue under diminished pressure the desired mpound is obtained as a colorless liquid, b. p. 164–7°/14 mm. which nnot be obtained free from traces of the parent arsine. By gently iling for three hours with carbon bisulfide and aluminium chloride and bsequently decomposing with ice, As-methyltetrahydroarsinoline,



is produced.[219]

Methyl-γ-phenylpropylbromoarsine, prepared like the preceding com-ound, is a colorless liquid, b. p. 177–86°/16 mm.[219]

Basic diisoamylchloroarsine, $[(C_5H_{11})_2AsCl]_6.[(C_5H_{11})_2As]_2O$.—A ixture of 2 moles of isoamyl chloride and one of arsenic trichloride is owly added to 4 atomic equivalents of sodium in dry ether in an mosphere of carbon dioxide. The reaction, which is very violent, is

complete in two hours. The filtered solution is fractionated, a white, soapy solid, probably diisoamylarsineoxide, separating. The red by-product, invariably formed during the above condensation, probably resembles Bunsen's "Erytrarsin," for when treated successively with bromine and ammonia it dissolves to form the ammonium salts of arsenious, isoamylarsonic and diisoamylarsinic acids.

Basic diisoamylchloroarsine is a colorless oil, b. p. 263°/750 mm., 148°/33 mm.; has a peculiar, characteristic odor less intense than cacodyl chloride; is soluble in the usual organic solvents but insoluble in water. With bromine in dry ether it forms diisoamylarsinechlorodibromide, $(C_5H_{11})_2AsCl.Br_2$.[220]

Diethoxychloroarsine, $(C_2H_5O)_2AsCl$, is prepared by regulating the action of sodium ethoxide upon arsenic trichloride. A solution of 30 g. of metallic sodium in 600 c.c. of alcohol is slowly added to 118 g. of arsenic trichloride. This requires about two and one-half hours. After standing for twenty four hours at ordinary temperature, the mixture is warmed for one hour, the sodium chloride separated, the excess alcohol removed, and the residual liquid distilled under diminished pressure.[221] The product is a colorless liquid boiling at 64–5°/20 mm., 159–60°/760 mm., and forming a precipitate of arsenic trioxide with water.

Di(β-chlorovinyl)chloroarsine, $(CHCl=CH)_2AsCl$, is one of the products formed during the interaction of acetylene and arsenic trichloride in the presence of aluminium chloride. It is a colorless or pale yellow liquid, b. p. 130–33°/26 mm., 108°/7 mm., or 250° at ordinary pressure. It has less marked vesicant properties than the corresponding primary compound but is a more intense respiratory irritant. It is insoluble in water or dilute acids, soluble in the common organic solvents. It forms additive compounds with halogens, and is oxidized by nitric acid to a crystalline substance melting at 97°.[175]

Dimethylcyanoarsine (Cacodyl cyanide), $(CH_3)_2AsCN$, may be prepared by distilling cacodyl oxide with concentrated hydrocyanic acid:

$$[(CH_3)_2As]_2O + 2HCN \longrightarrow 2(CH_3)_2AsCN + H_2O.$$

The product thus obtained is contaminated with unchanged cacodyl oxide, the removal of which is very difficult because of the great oxidizability and terribly poisonous character of the cyanoarsine. A better method consists in treating cacodyl oxide with concentrated mercuric cyanide solution and subsequently distilling:

$$[(CH_3)_2As]_2O + Hg(CN)_2 \longrightarrow 2(CH_3)_2AsCN + Hg.$$[222]

Recently it has been prepared by heating cacodyl oxide with five times the calculated amount of dry hydrocyanic acid in a sealed tube for two hours at 100°, removing the excess of hydrocyanic acid by a current of carbon dioxide and distilling the residue, cacodyl cyanide coming over at 160°.[223]

The product has a remarkable capacity for crystallizing in lustrous, colorless prisms melting at 33°, boiling at 140° and readily subliming at ordinary temperature. When heated in air it burns with a violet flame. It is the most poisonous compound of the cacodyl series, the inhalation of air containing only a very slight amount, rapidly producing numbness of the extremities, giddiness, stupor, and finally leading to complete unconsciousness. These symptoms, however, are merely transient and without after-effects, providing exposure to this compound has not been unduly prolonged. It is slightly soluble in water, readily in ether or alcohol. Heating with methyl iodide for two hours at 100° in an atmosphere of carbon dioxide converts it into tetramethylarsonium iodide and -triiodide.

On boiling cacodyl cyanide for 12 hours with dilute sulfuric acid, it is converted into dimethylarsinoformic acid, $(CH_3)_2As.COOH$, which is isolated through the calcium salt. The free acid reddens blue litmus paper and forms stable sodium, calcium, magnesium, manganese, iron, cerium, mercury, quinine and strychnine salts.[224]

Diethylcyanoarsine results on heating triethylarsine cyanobromide up to 110° in a sulfuric acid-bath under 12 mm. pressure, the diethylcyanoarsine coming over at 74°/12 mm. It is purified by rectification, has a typical cacodylic odor, and melts at —50°.[225]

Diisobutylcyanoarsine, b. p. 116°/16 mm., is formed on heating ethyldiisobutylarsine cyanobromide.[226]

Dimethylthiocyanoarsine (Cacodyl thiocyanate), $(CH_3)_2As.CNS$, from cacodyl chloride and sodium thiocyanate in acetone solution, is a colorless oil which gradually turns yellow, has a strongly irritating odor, and is readily soluble in alcohol, ether, benzene or acetone.[227]

3. *Dialkyl Arsineoxides,* $(R_2As)_2O$.—Compounds of this type may be regarded as anhydrides of dialkylated arsenious acids:

$$\mathrm{As}\begin{cases}\mathrm{OH}\\ \mathrm{OH}\\ \mathrm{OH}\end{cases} \longrightarrow \mathrm{As}\begin{cases}\mathrm{R}\\ \mathrm{R}\\ \mathrm{OH}\end{cases}$$

$$2R_2AsOH \xrightarrow{-H_2O} R_2As.O.AsR_2.$$

Up to the present time but two members of this series are known, dimethyl- and diisoamylarsineoxides. The former, together with cacodyl,

was first prepared by Cadet [228] in 1760 and is the foundation upon which rests the development of the organic compounds of arsenic. It constitutes the major portion of "Cadet's fuming arsenical liquid" prepared by the dry distillation of arsenic trioxide with potassium acetate according to the following equation:

$$4CH_3COOK + As_2O_3 \longrightarrow [(CH_3)_2As]_2O + 2K_2CO_3 + 2CO_2.$$

The subsequent investigations of Thénard,[6] Bunsen [229] and J. B. Dumas,[230] however, established the fact that the above equation does not quantitatively represent the course of the reaction, for in addition there occurs reduction of some of the arsenic trioxide to metallic arsenic, charring of a portion of the potassium acetate accompanied by evolution of methane and unsaturated hydrocarbons, and reduction of a slight amount of cacodyl oxide to cacodyl, the latter furnishing Cadet's liquid with its fuming and inflammable characteristics.

The dialkylarsine oxides are obtained

1. From the corresponding halogenated arsines by treatment with caustic potash solution:

$$2R_2AsX + 2KOH \longrightarrow (R_2As)_2O + 2KX + H_2O.$$

2. By the partial oxidation of dialkylarsines on exposure to air:

$$2R_2AsH + O_2 \longrightarrow (R_2As)_2O + H_2O.$$

Unlike the arsines, the oxides are not inflammable in air, but are readily converted into arsinic acids by oxidizing agents. They are insoluble in water, readily soluble in organic solvents, and form double salts with mercury and platinum salts.

Dimethylarsineoxide (*Cacodyl oxide*), $[(CH_3)_2As]_2O$, is isolated in pure form from the crude arsenical liquid of Cadet, by first converting it into the corresponding chloride by distilling with mercuric chloride and hydrochloric acid. The cacodyl chloride is dried with calcium chloride, freed from excess hydrochloric acid with powdered calcium carbonate, rectified, and finally distilled with aqueous sodium- or potassium hydroxide, the cacodyl oxide passing over in steam. The oily distillate, when dried and rectified in an atmosphere of carbon dioxide, yields the pure oxide as a colorless oil, sp. gr., 1.462/15°; b. p. 120°.[231] It crystallizes in scales at —25°, does not fume or ignite in air, has an intolerable tear-exciting odor, and is sparingly soluble in water. With oxidizing agents such as mercuric oxide, it forms dimethylarsinic acid, the latter being reconverted into the arsineoxide by reduction with phosphorous acid. Although it reacts neutral, the oxide yields the corresponding halides when distilled with concentrated haloid acids.

The mercurichloride, $[(CH_3)_2As]_2O.2HgCl_2$, prepared from its components in alcoholic solution, consists of rhombic plates soluble in alcohol

or hot water and yields cacodyl chloride upon distillation with concentrated hydrochloric acid; the corresponding mercuribromide, similarly prepared, is a white crystalline powder possessing the same solubilities as the chloride; while the platinichloride, $[(CH_3)_2As]_2O.PtCl_2.H_2O$, obtained as colorless needles by recrystallizing cacodyl chloride-platinichloride from boiling water, may be transposed with potassium bromide or -iodide, silver nitrate or -sulfate, yielding the following compounds respectively: $[(CH_3)_2As]_2O.PtBr_2.H_2O$, colorless crystals; $[(CH_3)_2As]_2O.PtI_2.H_2O$, fine, yellow scales; $[(CH_3)_2As]_2O.Pt(NO_3)_2.H_2O$; and $[(CH_3)_2As]_2O.PtSO_4.H_2O$.

Diisoamylarsineoxide, $[(C_5H_{11})_2As]_2O$, is a white, soapy solid formed in the preparation of basic diisoamylchloroarsine,[232] or by the oxidation of diisoamylarsine in air.[193]

4. *Dialkyl Arsinesulfides*, $[R_2As]_2S$.—The same relationship exists between these compounds and the corresponding arsineoxides as that observed in the case of the primary arsinesulfides and -oxides. They are obtained:

1. From secondary aliphatic arsines by heating with sulfur:

$$2R_2AsH + S_2 \longrightarrow (R_2As)_2S + H_2S.$$

With an excess of sulfur, however, the corresponding disulfide is produced:

$$2R_2AsH + 3S \longrightarrow (R_2As)_2S_2 + H_2S.$$

2. From secondary halogenated arsines by treating with barium hydrosulfide or hydrogen sulfide:

$$2R_2AsX + Ba(SH)_2 \longrightarrow (R_2As)_2S + H_2S + BaX_2$$
$$2R_2AsX + H_2S \longrightarrow (R_2As)_2S + 2HX.$$

3. By the action of barium hydrosulfide upon secondary arsineoxides in acid solution:

$$(R_2As)_2O + 2CH_3COOH + Ba(SH)_2 \longrightarrow (R_2As)_2S + (CH_3COO)_2Ba + H_2S + H_2O.$$

4. Upon reduction of dialkyl arsinic acids by means of hydrogen sulfide:

$$2R_2AsO.OH + 3H_2S \longrightarrow (R_2As)_2S + S_2 + 4H_2O.$$

Only two dialkylarsinesulfides are known, the dimethyl and diisoamyl compounds, both of which are insoluble in alcohol or ether.

Dimethylarsinesulfide (Cacodyl sulfide), $[(CH_3)_2As]_2S$.—Prepared by passing hydrogen sulfide through a concentrated alcoholic solution of cacodylic acid;[233] by distilling cacodyl chloride with barium hydro-

sulfide;[234] from the acid upper layer obtained in Cadet's distillation by treating with the same reagent,[235] the latter reaction proceeding according to the equation:

$$[(CH_3)_2As]_2O + 2CH_3COOH + Ba(SH)_2 \longrightarrow [(CH_3)_2As]_2S + (CH_3COO)_2Ba + H_2O + H_2S.$$

Finally, it may be prepared by heating dimethylarsine (2 moles) with less than one mole of sulfur in a sealed tube, and allowing to stand for two or three days. The resulting liquid consists of a mixture of cacodyl sulfide and trimethylarsine sulfide, which are separated by fractional distillation.[236]

Cacodyl sulfide is a colorless oil with a repulsive odor resembling those of mercaptan and cacodyl oxide. It boils at 211°, is distillable in steam, insoluble in water, miscible with alcohol or ether, and is decomposed by hydrochloric acid, forming cacodyl chloride and hydrogen sulfide. It inflames in the air, burning with a pale arsenic flame. With sulfur in alcoholic solution the disulfide, $[(CH_3)_2As]_2S_2$, is obtained; with oxygen cacodylic acid results, while with cupric nitrate in alcoholic solution it yields well-defined, lustrous octahedra of the cuprisulfide, $[(CH_3)_2As]_2S.3CuS$.[237, 238]

Diisoamylarsinesulfide, $[(C_5H_{11})_2As]_2S$, prepared by passing hydrogen sulfide through a suspension of the corresponding chloride in water, forms white needles, m. p. 29–30°, readily soluble in ether or carbon bisulfide, sparingly in alcohol and insoluble in water.[239]

Dimethylarsinedisulfide (*Cacodyl disulfide*), $[(CH_3)_2As]_2S_2$, may be prepared either by the direct union of cacodyl sulfide and sulfur,[240] or from dimethylarsine and an excess of sulfur in a sealed tube at ordinary temperature.[236] It crystallizes either in the form of small prisms or rhombic plates, m. p. 50°, readily soluble in alcohol, but sparingly in ether.

Dimethylarsineselenide (*Cacodyl selenide*), $[(CH_3)_2As]_2Se$, is made by distilling cacodyl chloride with aqueous sodium selenide:

$$2(CH_3)_2AsCl + Na_2Se \longrightarrow [(CH_3)_2As]_2Se + 2NaCl.$$

It is a transparent, yellow liquid with a repulsive, penetrating odor; is insoluble in water, readily soluble in alcohol or ether, and burns in air with a blue flame, evolving selenium dioxide.[241]

5. *Tetraalkyldiarsines* (*Cacodyl Compounds*), $R_2As—AsR_2$.—The cacodyls may be considered as secondary arsines whose hydrogen has been removed:

$$2R_2AsH \xrightarrow{-H_2} R_2As—AsR_2.$$

They may be prepared:

1. From secondary halogenated arsines by heating with zinc:

$$2R_2AsX + Zn \longrightarrow (R_2As)_2 + ZnX_2.$$

2. By condensing secondary arsines with secondary halogenated arsines:

$$R_2AsH + R'_2AsX \longrightarrow R_2As.AsR'_2 + HX.$$

3. From arsinic acids by reduction with hypophosphorous acid.

4. In small yields by the interaction of alkyl iodides and sodium arsenide.

The products are heavy, oily liquids with a repulsive odor; are sparingly soluble in water, and very easily oxidized, the methyl and ethyl compounds igniting spontaneously in air. They combine directly with oxygen, sulfur, halogens or alkyl halides, the latter producing tetraalkyl arsonium compounds and dialkyl halogenated arsines:

$$\begin{array}{ccccc} R_2As - AsR_2 & \xrightarrow{R'X} & \begin{array}{ccc} R_2As & \vdots & AsR_2 \\ | & \vdots & | \\ X & \vdots & R' \end{array} & \longrightarrow & R_2AsX + R_2R'As \\ & & & & \Big\downarrow {\scriptstyle R'X} \\ & & & & R_2R'_2AsX. \end{array}$$

Tetramethyldiarsine (*Cacodyl*), $(CH_3)_2As.As(CH_3)_2$.—As has already been mentioned, this substance is one of the constituents of "Cadet's arsenical liquid." The pure compound may be obtained by heating cacodyl chloride with zinc at 90–100° in an atmosphere of carbon dioxide.[242] It is also formed upon reducing cacodylic acid either in hydrochloric acid solution with hypophosphorous acid,[243] or in 2 N-sulfuric acid by an electrolytic method;[244] and in small amounts, together with trimethylarsine and tetramethylarsonium iodide, from methyl iodide and sodium arsenide.[245]

It is a colorless, highly refractive oil with a repulsive odor; is heavier than water in which it is but slightly soluble; boils at 170°, decomposes at 400-500°, yielding arsenic and hydrocarbons but no free carbon, and solidifies at — 6°, forming crystals. It inflames spontaneously in air or in an atmosphere of chlorine, but by regulated oxidation with moist air or preferably mercuric oxide, it yields successively cacodyl oxide and cacodylic acid. It also combines with sulfur and halogens, while with alkyl halides tetraalkylarsonium halides result.[246] According to Cahours, the products obtained with methyl bromide are tetramethylarsonium bromide and dimethylbromoarsine. Recently, however, Steinkopf and Schwen[247] showed that upon heating cacodyl with methyl bromide in a sealed tube filled with carbon dioxide for three hours at 100°, a mixture of tetramethylarsonium bromide and trimethylarsine hydroxybromide are obtained. With 2 moles of methyl iodide in a sealed tube filled with

carbon dioxide, cacodyl reacts at low temperature to form tetramethylarsonium iodide, while with 5 moles of methyl iodide under similar conditions, both tetramethylarsonium iodide and -triiodide are obtained.[247] Ethyl, amyl and allyl halides also react with cacodyl, yielding respectively dimethyldiethyl-, dimethyldiamyl- and dimethyldiallyl arsonium halides together with cacodyl halide. When heated with methyl sulfide in a sealed tube at 150–60° for several hours, cacodyl yields methylarsinesulfide and cacodyl sulfide.

Tetraethyldiarsine (*Ethyl cacodyl*) is made by mixing sodium arsenide with four to five times its weight of quartz sand, and refluxing with ethyl iodide in an atmosphere of carbon dioxide. When the reaction is completed, the whole is cooled, extracted with ether in an atmosphere of carbon dioxide, and the extract mixed with absolute alcohol. The ether is quickly removed and the alcoholic residue diluted with oxygen-free water, whereupon ethyl cacodyl separates as a pale yellow, very refractive oil, heavier than water, and boiling at 185–90°.[248] It has an unpleasant garlicky odor; is insoluble in water, slightly soluble in alcohol or ether, and oxidizes very rapidly in air, bursting into a flame which gives off arsenic trioxide. Concentrated nitric acid completely oxidizes it with generation of light and heat; while with dilute nitric acid there is obtained a light red powder, analogous to Bunsen's "Erytrarsin," which slowly turns brown, and on exposure to the air finally becomes white. Unlike triethylarsine, ethyl cacodyl has a powerful reducing action on salts of silver, mercury and the noble metals. It also combines directly with oxygen, sulfur or halogens, and differs from other alkyl cacodyls in that when incompletely ignited it always yields as a secondary product the red substance analogous to Bunsen's "Erytrarsin."

Dimethyldiisoamyldiarsine, $(CH_3)_2As.As(C_5H_{11})_2$.—When equimolar quantities of dimethylarsine and diisoamylchloroarsine are brought together in a sealed tube filled with carbon dioxide, no change is apparent to the eye even after heating for five hours at 100°, but on opening the tube no pressure is observed, showing the absence of any free dimethylarsine. The contents when treated with water yields the cacodyl compound as a fuming oil possessing the odor of amylarsine. The reaction evidently proceeds according to the equation:

$$(CH_3)_2AsH + (C_5H_{11})_2AsCl \longrightarrow (CH_3)_2As.As(C_5H_{11})_2 + HCl.$$[249]

Wöhler,[16] on distilling a mixture of equal parts by weight of potassium butyrate and arsenic trioxide, obtained a mixture of two liquids together with a considerable amount of reduced arsenic and some malodorous gas. The heavier oily liquid, although not spontaneously inflammable, burned with a white, smoky flame, giving off an arsenical odor, and yielded a white crystalline precipitate with mercuric chloride. On

boiling the liquid with zinc and hydrochloric acid, an odor resembling that of cacodyl was evolved, while boiling with concentrated hydrochloric acid alone produced a pungent odor affecting the mucous membranes of the eyes and nose. These reactions are highly suggestive of a cacodyl derivative, but the exact composition of the compound has not been ascertained.

W. Gibbs[17] obtained similar inconclusive results on distilling equal parts by weight of potassium valerate and arsenic trioxide. The product consisted of a heavy, pale yellow, oily liquid having an unpleasant odor, and fuming in air without inflaming. It yielded a heavy white precipitate with mercuric chloride, reduced mercuric oxide to the metal, and formed a crystalline solid on exposure to air.

C. Tertiary Derivatives.

1. *Trialkyl Arsines,* R_3As.—The members of this class of compounds correspond to hydrogen arsenide with the three hydrogen atoms replaced by alkyl groups. Although arsine itself cannot be employed directly in the synthesis of such derivatives, its trihalides furnish suitable starting materials, the three halogen atoms being directly replaced by alkyl radicals upon interaction with either zinc dialkyls or alkylmagnesium iodides. The trialkyl arsines result:

1. From the interaction of zinc dialkyls or alkylmagnesium halides and arsenic trichloride:

$$3ZnR_2 + 2AsX_3 \longrightarrow 3ZnX_2 + 2R_3As$$
$$3RMgX + AsX_3 \longrightarrow R_3As + 3MgX_2.$$

2. From primary or secondary halogenated arsines and zinc dialkyls:

$$RAsX_2 + ZnR'_2 \longrightarrow RR'_2As + ZnX_2$$
$$2R_2AsX + ZnR'_2 \longrightarrow 2R_2R'As + ZnX_2.$$

3. By the interaction of sodium arsenide and alkyl iodides:

$$Na_3As + 3RI \longrightarrow R_3As + 3NaI.$$

4. Upon decomposing tetraalkyl arsonium halides by distillation with solid caustic potash:

$$R_4AsX \longrightarrow R_3As + RX.$$

5. By treating secondary arsines with alkyl halides and decomposing the resulting salt with water:

$$R_2AsH + R'X \longrightarrow R_2R'As.HI \xrightarrow{H_2O} R_2R'As + HI.$$

The products are all colorless liquids of repulsive odor, soluble in alcohol or ether. They possess basic properties, forming haloid salts which are quite stable in dry air but are decomposed by water. With halogens, oxygen or sulfur they readily combine to form the correspond-

ing dihalides, oxides or sulfides, while with alkyl halides they readily form arsonium compounds. By heating in sealed tubes at high temperatures, the tertiary arsines decompose, yielding compounds of the type $(RAs)_4$ and higher aliphatic hydrocarbons.

Trimethylarsine, $(CH_3)_3As$, is prepared by distilling tetramethylarsonium iodide or its double salt, $(CH_3)_4AsI.AsI_3$, with solid potassium hydroxide;[250] from methyl magnesium iodide and arsenic tribromide in ether solution,[251] unsatisfactory results being obtained with arsenic trichloride;[252] or from zinc dimethyl and arsenic trichloride.[253, 254] If the last method is carried out in anhydrous ether medium, a white solid is obtained which is first dissolved in water, an excess of concentrated alkali added, and the whole distilled on a water bath. The distillate upon fractionation yields but a small amount of trimethylarsine, apparently on account of the fact that ether and trimethylarsine form a mixture difficult to separate by fractionation, for upon repeating the experiment with xylene as a diluent, the yield obtained is much more satisfactory. Trimethylarsine may also be obtained together with $(CH_3As)_4$ by heating crude cacodyl for two hours at 340° in a sealed tube filled with carbon dioxide,[255] or as a by-product during the interaction of sodium arsenide and methyl iodide, the main product being tetramethylarsonium iodide.[245]

The compound is a colorless, highly refractive liquid, boiling below 100°, and possessing a sickening, garlicky odor. With an excess of mercuric chloride solution, it forms a voluminous white precipitate of the double salt, $[(CH_3)_3As]_2.HgCl_2$, which when recrystallized from hot water separates as pearly-white leaflets. The arsine combines with oxygen, yielding the corresponding arsine oxide; with sulfur the arsine sulfide results, while with an excess of bromine in ethereal solution, a red arsine perbromide is formed.

Triethylarsine is derived from arsenic trichloride and zinc diethyl;[253, 256] from tetraethylarsonium iodide or the double salt, $(C_2H_5)_4AsI.AsI_3$, by distillation with solid caustic potash;[257] and together with ethyl cacodyl and tetraethylarsonium iodide by mixing sodium arsenide with quartz sand and warming with ethyl iodide in a reflux apparatus.[258] A very satisfactory method consists in adding an ethereal solution of arsenic trichloride to a strongly-cooled solution of ethylmagnesium bromide in the same solvent, and decomposing the reaction product with ice and hydrochloric acid. The ethereal layer is then removed, dried with calcium chloride, and the solvent distilled off in an atmosphere of carbon dioxide, the last traces in vacuo. From the residual liquid, triethylarsine is obtained by first distilling in vacuo and then rectifying the distillate in an atmosphere of carbon dioxide. It is preserved in sealed ampules filled with carbon dioxide.[259]

The substance is a colorless, fuming liquid with an unpleasant odor, b. p. 140°/736 mm.; sp. gr., 1.151/16.7°; insoluble in water but miscible with alcohol and ether. Heating at 265° for three hours decomposes it according to the equation:

$$4(C_2H_5)_3As \longrightarrow (C_2H_5As)_4 + 4C_4H_{10}.$$

With mercuric chloride in alcoholic solution, it forms white needles readily soluble in alcohol or hot water, and decomposed by ammonia with the precipitation of mercurous oxide. The arsine dissolves in dilute nitric acid, forming triethylarsine nitrate; does not reduce the oxides of the noble metals, but on warming with concentrated sulfuric acid the latter is reduced to sulfurous acid. It forms addition products with halogens, sulfur or oxygen. With platinic chloride, two isomeric varieties of the double salt, $2(C_2H_5)_3.PtCl_2$, are obtained, which may be separated by extraction with ether. The ether soluble variety crystallizes in amber-yellow crystals, while the insoluble variety crystallizes from hot alcohol in long, pale yellow prisms. These isomers are analogous to those obtained from triethylphosphine and platinic chloride. With palladium chloride, triethylarsine forms transparent, orange-yellow prisms of $2(C_2H_5)_3As.PdCl_2$, while aurous chloride yields colorless prisms of $(C_2H_5)_3As.AuCl$. In preparing the latter it is necessary to avoid too high a temperature, as reduction to metallic gold occurs.[260]

Tri-n-propylarsine, an oil boiling at 167°/90 mm., 158°/73 mm., is prepared by distilling the double iodide, $(C_3H_7)_4AsI.AsI_3$, with dry potassium hydroxide,[261] or by condensing n-propyl chloride and arsenic trichloride with metallic sodium in ether, primary and secondary n-propyl derivatives being obtained as by-products.[262] When heated for two hours at 295°, a polymer $(C_3H_7As)_4$ is obtained:

$$4(C_3H_7)_3As \longrightarrow (C_3H_7As)_4 + 4C_6H_{14}.$$

Dimethylethylarsine, $(CH_3)_2(C_2H_5)As$, from cacodyl iodide and an excess of zinc diethyl by heating in a sealed tube on a water-bath, is a colorless mobile liquid with a disgusting odor resembling that of trimethylarsine.[263]

Dimethyl-n-propylarsine hydriodide, $(CH_3)_2(C_3H_7)As.HI$, is obtained by permitting n-propyl iodide and dimethylarsine to react for a number of days in a sealed tube filled with carbon dioxide.[264]

Dimethyl-γ-phenylpropylarsine, $(CH_3)_2(C_6H_5.C_3H_6)As$, a colorless, highly refractive liquid boiling at 133°/14 mm., is prepared by slowly adding a benzene solution of dimethyliodoarsine to an ethereal solution of γ-phenylpropylmagnesium bromide and warming for one hour. With dimethyliodoarsine it forms an additive compound, $(CH_3)_2(C_6H_5.C_3H_6)As.(CH_3)_2AsI$, which crystallizes from ether, methyl alcohol or

concentrated hydrochloric acid in colorless prisms melting at 78–81°, and completely dissociating into its components in benzene.[265]

Dimethylallylarsine, $(CH_3)_2(C_3H_5)As$, from dimethylarsine and allyl iodide, is a pale yellow liquid with a disagreeable odor, b. p. 160°. With bromine in ether solution it forms the corresponding arsine dibromide.[266]

Methyldiethylarsine, $(CH_3)(C_2H_5)_2As$, resulting from the interaction of methyldiiodoarsine and an excess of zinc diethyl in a sealed tube at water-bath temperature, is a colorless liquid of very unpleasant odor, heavier than water, and readily forming additive compounds with halogens or sulfur.[267]

Ethyldi-n-propylarsine, $(C_2H_5)(C_3H_7)_2As$, from n-propylmagnesium bromide and ethyldichloroarsine in an oxygen-free atmosphere, is a refractive liquid boiling at 60-64°/14 mm.[268]

Ethyldiisobutylarsine, $(C_2H_5)(C_4H_9)_2As$, similarly prepared from isobutylmagnesium bromide in ethereal solution, is a colorless, highly refractive liquid, b. p. 86°/16 mm.[269]

Tri(β-chlorovinyl)arsine, $(CHCl{=}CH)_3As$, is obtained together with the corresponding primary and secondary chloroarsines on condensing acetylene with arsenic trichloride in the presence of aluminium chloride. It is a colorless liquid, b. p. 151–5°/28 mm., m. p. 3–4°, fairly stable in air, and insoluble in water, dilute acids or alcohol. It is neither a strong vesicant nor a powerful respiratory irritant, but induces violent sneezing.[175] Its double salt with aurous chloride, $(CHCl{=}CH)_3As.AuCl$, consists of small, heavy, white crystals, m. p. 123° with decomposition, and slowly turning purplish-gray on exposure to light. With palladous chloride in alcoholic solution the arsine forms an addition product, $[(CHCl{=}CH)_3As]_2.PdCl_2$, long, yellowish-brown needles soluble in ether or acetone, and melting at 196° with decomposition. With chloroplatinic acid in aqueous alcoholic solution there is obtained a mixture of long, pale yellow needles and lemon-yellow prisms. By agitating this mixture with benzene, there remains a crystalline substance probably corresponding to the formula, $[(CHCl{=}CH)_3As]_2Pt(CH{=}CHCl)_2$, which separates from alcohol in almost white needles and from benzene in pale plates, m. p. 198° with decomposition. When the arsine is carefully treated with nitric acid it yields a hydroxynitrate, $(CHCl{=}CH)_3As{<}^{OH}_{NO_3}$, m. p. 103°, which may be converted into the corresponding arsineoxide by treating its aqueous solution with caustic soda. On boiling an acetone solution of the arsine with Chloramine T (1 mole) for 20 minutes, there is formed a compound $(CHCl{=}CH)_3As{=}N.SO_2C_6H_4(CH_3).H_2O$, consisting of colorless plates melting at 124°.[270]

Chapter II. Pentavalent Aliphatic Compounds.

A. Primary Derivatives.

1. *Alkyl Arsinetetrahalides*, $RAsX_4$.—Compounds of this type may be regarded either as arsonic acids with the oxygen and hydroxyl groups replaced by halogens, or as arsenic pentahalides with one of the halogens replaced by an alkyl radical:

$$RAs\begin{matrix} /\!\!/ O \\ -OH \\ \diagdown OH \end{matrix} \longrightarrow RAs\begin{matrix} \diagup X \\ -X \\ \diagdown X \\ \diagdown X \end{matrix} \longleftarrow AsX_5.$$

Very little work has been done on this class of compounds, methylarsinetetrachloride and -tetraiodide being the only derivatives prepared to date. They are both unstable at room temperature and can only be preserved at $-10°$ or below.

Methylarsinetetrachloride, CH_3AsCl_4, prepared by passing chlorine through a mixture of methyldichloroarsine and carbon bisulfide at $-10°$, is obtained in large crystals which cannot be separated from the liquid, as they decompose with the evolution of a gaseous product as the temperature approaches 0°. The reactions involved are:

$$CH_3AsCl_2 + Cl_2 \longrightarrow CH_3AsCl_4 \longrightarrow AsCl_3 + CH_3Cl.$$ [271]

Methylarsinetetraiodide is made by the action of concentrated hydriodic acid upon sodium methylarsonate.[163] It crystallizes in red-brown, hexagonal plates, which form a beautifully crystalline compound with trimethylsulfonium iodide, and yield methyldiiodoarsine with sulfurous acid.

2. *Alkyl Arsonic Acids.*—The members of this chapter are theoretically derived from arsenic acid, $AsO(OH)_3$, by replacing one of the hydroxyl groups by an alkyl radical, and may be represented by the structural formula, $R-As\begin{matrix} /\!\!/ O \\ -OH \\ \diagdown OH \end{matrix}$. The proof of the direct union of carbon with arsenic lies in their ready reduction to the corresponding

arsines, which unquestionably contain such direct carbon-arsenic linkage and which may be very easily reoxidized to the arsonic acids.

$$\begin{cases} RAsO(OH)_2 + 6H \longrightarrow RAsH_2 + 3H_2O. \\ RAsH_2 + 3O \longrightarrow RAsO(OH)_2. \end{cases}$$

That the arsenic is in the pentavalent condition may be deduced from the stability of the arsonic acids toward such oxidizing agents as nitric acid, chlorine or bromine, which readily oxidize all trivalent arsenicals. The above structural formula also indicates the presence of two hydroxyl groups, which is borne out by the fact that the acids form salts with alkalis containing either one or two atoms of the metal.

Several methods are available for the preparation of aliphatic arsonic acids:

1. Hydrolysis of the corresponding alkyl arsineoxyhalides or -tetrahalides:

$$RAsOX_2 + 2H_2O \longrightarrow RAsO(OH)_2 + 2HX$$
$$RAsX_4 + 3H_2O \longrightarrow RAsO(OH)_2 + 4HX.$$

2. Oxidation of primary aliphatic dihalogenated arsines by means of moist silver oxide or hydrogen peroxide:

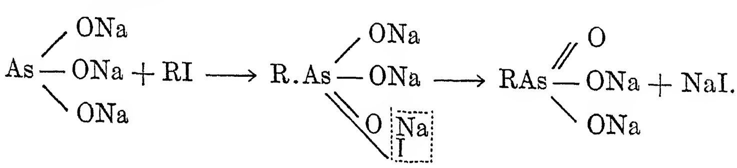
$$RAsX_2 + Ag_2O + 2H_2O \longrightarrow RAsO(OH)_2 + 2HX + 2Ag$$
$$RAsX_2 + 2H_2O_2 \longrightarrow RAsO(OH)_2 + 2HX + O.$$

3. Oxidation of alkylarsines by atmospheric oxygen:

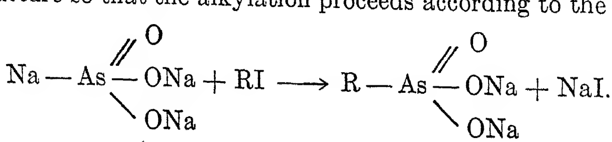
$$2RAsH_2 + 3O_2 \longrightarrow 2RAsO(OH)_2.$$

4. The reaction of alkyl halides with alkali arsenites.

The last method is theoretically the most interesting of all and can be readily employed on an industrial scale. It was devised by G. Meyer [33] and is dependent upon the fact that alkyl iodides first combine additively with sodium arsenite in alkaline solution, producing compounds in which the arsenic exists in a pentavalent condition. These intermediate products then lose one molecule of alkali iodide, forming a dialkali arsonate:



It is also possible that in this reaction sodium arsenite assumes a tautomeric structure so that the alkylation proceeds according to the equation:



This method was modified by Klinger and Kreutz [34] and later elaborated and extended by Dehn.[272] The latter performed a number of interesting experiments in order to determine the most favorable conditions and the extent of its applicability. As a result, the following procedure was found most satisfactory: the alkali arsenite is treated with the alkyl iodide in sufficient water and alcohol to insure homogeneous solution, and after reacting either at ordinary temperature or at higher temperature in sealed tubes the solution is evaporated to dryness on a water-bath, the residue dissolved in water, feebly acidified with dilute sulfuric acid and rendered alkaline with sodium bicarbonate. The amount of unchanged arsenite may be determined by titrating the final solution with iodine, the alkyl arsonic acids remaining unaffected. In addition, Dehn noted the following facts in connection with this procedure: 1. That the reaction is almost complete in one hour and entirely so at the end of twenty four hours; 2. That by employing potassium instead of sodium arsenite much less alcohol is required and the yield is practically doubled; 3. That the alkyl bromides are not as well adapted for alkylation as the iodides; 4. That although alkylation continues to take place with the higher alkyl halides, the yields vary inversely as their molecular weights.

The method as developed by Dehn is generally applicable to the preparation of the primary aliphatic arsonic acids with very good yields. Valeur and Delaby [273] recently reinvestigated this modification of Meyer's method, and found that in aqueous-alcoholic solution potassium arsenite is converted into the arsonate much less rapidly than indicated by Dehn. Furthermore, in preparing ethylarsonic acid by means of ethyl iodide, over 50 per cent of the latter is converted into ethyl ether by reacting with the ethyl alcohol present, thereby necessitating a large excess of alkyl iodide to completely utilize all of the arsenite. By carrying out the reaction in aqueous medium, however, without the addition of any alcohol, the disappearance of the theoretical quantity of ethyl iodide is parallel with the formation of potassium ethylarsonate. In addition, the speed of the reaction can be improved either by employing more vigorous agitation and efficient refrigeration or by operating under pressure.

Quick and R. Adams,[274] in preparing the higher aliphatic arsonic acids according to the method of Meyer, found the isolation of the products difficult because the sodium salts thus obtained are soluble in dilute alcohol and do not crystallize from the reaction mixture. Hence, they employed alkyl bromides or chlorides instead of iodides, so that the free arsonic acids may be isolated directly upon acidification; this is not possible when an alkyl iodide has been used, because the liberated hydriodic acid immediately reduces the arsonic acid. They adopted several suggestions of Valeur and Delaby, using water alone as the solvent, with heating and stirring to hasten the reaction. To isolate the

arsonic acid the solution was concentrated, the alkali halide filtered off, and the filtrate acidified. With the higher, less soluble homologues it is not even necessary to concentrate the reaction mixture, as precipitation occurs immediately upon acidification with hydrochloric acid.

The acids and their salts are, as a rule, beautiful, white, crystalline substances easily soluble in water or hot alcohol but insoluble in ether. The solubilities decrease with increasing molecular weights, while the melting points, on the other hand, increase.

Methylarsonic acid, $CH_3AsO(OH)_2$, may be obtained by keeping sodium arsenite and methyl iodide in dilute alcoholic solution in a closed vessel at ordinary temperature for several days and isolating through the sodium salt,[275] or better, by heating the components at 75° for several hours and isolating through the calcium salt.[33] The acid may also be derived from methyldichloroarsine by treatment with moist silver oxide or from methylarsineoxide and mercuric oxide, the product being isolated in both methods through the barium salt.[276] Finally, it results upon oxidation of methylarsine.[277]

The compound crystallizes from absolute alcohol in long, spear-shaped plates unaffected by dry air and very soluble in water or absolute alcohol, more so than cacodylic acid. It is a strong acid capable of decomposing carbonates, and has a pleasant acid taste. Its metallic salts are generally crystalline. It also forms an ammonium salt, which is not the case with cacodylic acid. It yields a precipitate with magnesia mixture in ammoniacal solution only upon warming, a distinction from arsenic acid which is characteristic of both aliphatic and aromatic arsonic acids in general.

Salts.—The disodium salt, $CH_3AsO(ONa)_2.6H_2O$, is a white crystalline powder readily soluble in water but sparingly in alcohol. It has been employed in medicine under the name of "Arrhenal." With an equimolar amount of mercury salicylate it forms a water-soluble salt "Enesol." The monosodium salt, $CH_3AsO.OH.ONa.3H_2O$, prepared by concentrating an aqueous solution of equimolar quantities of the disodium salt and the free acid,[278] is not precipitated from aqueous solution by alcohol. It loses its water of crystallization at 130°. The dipotassium salt may be prepared like the disodium salt from potassium arsenite; the calcium salt, $CH_3AsO_3Ca.H_2O$, is made by warming together solutions of sodium methylarsonate and calcium chloride;[279] the magnesium salt, containing $5H_2O$, is easily soluble in acids but difficultly in water, and is prepared in a manner similar to the calcium salt; the barium salt, precipitated from aqueous solution by the addition of alcohol, consists of white needles containing 5 molecules of water of crystallization, and is much more soluble in warm water than the calcium and magnesium salts;[280] the disilver salt, obtained by treating an aqueous solution of barium or

disodium methylarsonate with silver nitrate,[281] forms lustrous crystals which contain no water of crystallization, remain unchanged at 100°, but decompose with strong detonation at higher temperature. It is quite stable in air and sunlight, and begins to darken only after long exposure. Mercurous, mercuric,[282] and iron salts [283] have also been prepared. Alkaloidal methylarsonates result upon mixing equimolar quantities of the alkaloidal sulfate and disodium methylarsonate to a thick paste with water, evaporating to dryness and extracting the desired salt from the residue with alcohol. The following salts have been thus prepared: strychnine, quinine, atropine, cinchonine, quinidine, brucine, pilocarpine, codeine, morphine, aconitine, narceine, papaverine, thebaine, narcotine, berberine, caffeine and heroine.[284] The yohimbine salt melts at 203°.[285] On boiling an aqueous solution of disodium methylarsonate with molybdenum trioxide and finally treating with an excess of guanidinium chloride, a mixture of two compounds is obtained — rectangular plates corresponding to the formula, $(CN_3H_6)_2\left[\overset{CH_3}{As}\,(Mo_2O_7)_3\right]11H_2O$, and needles of a compound, $(CN_3H_6)_8H_2\left[\begin{matrix}\overset{CH_3}{As}(Mo_2O_7)_4 & \overset{CH_3}{(Mo_2O_7)_4As} \\ \multicolumn{2}{c}{-Mo_2O_7-}\end{matrix}\right]8H_2O$.[286]

Diiodomethylarsonic acid, $(CHI_2)AsO(OH)_2$, is obtained together with bis(diiodomethyl)arsinic acid from amorphous arsenic with iodoform by warming in a neutral solvent such as benzene or toluene on a water-bath for several hours, and finally distilling off the solvent. A dense black, oily crystalline magma remains, which is oxidized in the cold by nitric acid, the resulting product extracted with cold water, filtered and the filtrate concentrated at 40-50°. The diiodo acid crystallizes out upon cooling. The residue remaining after the extraction with water is first boiled with benzene or toluene to remove free iodine, then dissolved in ammonia and the tetraiodocacodylic acid, $(CHI_2)_2AsO.OH$, reprecipitated with cold acetic or nitric acid:

$$3CHI_3 + 2As \longrightarrow CHI_2.AsI_2 + (CHI_2)_2AsI$$
$$CHI_2.AsI_2 + 4HNO_3 \longrightarrow CHI_2.AsO(OH)_2 + 4NO_2 + H_2O + I_2$$
$$(CHI_2)_2AsI + 3HNO_3 \longrightarrow (CHI_2)_2AsO.OH + 3NO_2 + H_2O + I.$$

Diiodomethylarsonic acid crystallizes with $1H_2O$ in the form of large, yellow, efflorescent tablets. When boiled with nitric acid, it is decomposed with liberation of iodine, the arsenic being oxidized to arsenic acid, while boiling with alkali decomposes it according to the equation:

$$CHI_2.AsO_3H_2 + 2NaOH \longrightarrow CH_2I_2 + Na_2HAsO_4 + H_2O.$$

The sodium salt, $CHI_2.AsO.OH.ONa.H_2O$, is soluble in water, but its white silver salt is insoluble.[287]

Pyrobismethylarsonic acid, $CH_3AsO(OH).O.(OH)OAsCH_3$, is prepared by heating methylarsonic acid at 130° in a current of hydrogen, one molecule of water being split off. At higher temperatures (170-80°) it decomposes into methyl alcohol and arsenious oxide. The corresponding sodium salt is obtained in a similar manner by heating monosodium methylarsonate. Water converts the salt as well as the acid into the corresponding arsonic acid derivative.[288]

Ethylarsonic acid, $C_2H_5AsO(OH)_2$, is prepared like the methyl derivative from potassium arsenite and ethyl iodide, and is finally precipitated as the magnesium salt, from which the free acid is obtained by decomposing with sulfuric acid and extracting with boiling alcohol.[272] A simpler method consists in employing ethyl bromide and sodium arsenite, the arsonic acid being subsequently precipitated with hydrochloric acid, thereby eliminating the precipitation with magnesia mixture.[289] The same compound has also been made either by digesting ethyldichloroarsine with dilute nitric acid on a water-bath and isolating through the potassium salt,[290] or by treating ethyldiiodoarsine with silver oxide.[291]

The product crystallizes from alcohol in beautiful white crystals melting at 99.5°, and readily soluble in water or alcohol. The sodium and potassium salts form colorless crystals soluble in hot alcohol; the magnesium salt consists of small globular masses easily soluble in acids, while the silver salt crystallizes in yellowish scales with a mother-of-pearl luster.

La Coste made an unsuccessful attempt to prepare glycylarsonic acid, $HOOCCH_2AsO(OH)_2$, by oxidizing ethylarsonic acid with potassium permanganate in alkaline solution, but instead the acid decomposed into acetic and arsenic acids.[292]

n-Propylarsonic acid, $C_3H_7AsO(OH)_2$, is made in the same manner as ethylarsonic acid by employing potassium arsenite and n-propyl iodide at ordinary temperature, some ethylpropyl ether being formed at the same time. The acid is isolated through its magnesium salt.[293] It may also be derived from sodium arsenite and n-propyl bromide.[289] The acid crystallizes in needles, m. p. 126-7°; soluble in water or alcohol but insoluble in ether.

Allylarsonic acid, $C_3H_5AsO(OH)_2$, m. p. 128-9°; is produced from sodium arsenite and allyl halides.[289, 294]

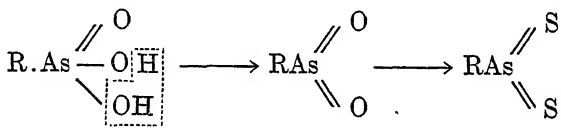
n-Butylarsonic acid, $C_4H_9AsO(OH)_2$, from n-butyl bromide and sodium arsenite, melts at 159-60° and resembles the other arsonic acids in general properties. It forms an insoluble magnesium salt with magnesia mixture.[289]

Isoamylarsonic acid, $C_5H_{11}AsO(OH)_2$, obtained from potassium arsenite and isoamyl iodide,[295] is a pearly white, crystalline substance melting at 194°; soluble in water or alcohol but insoluble in ether. By heating for four hours at 285° it decomposes thus:

$$2C_5H_{11}AsO_3H_2 \longrightarrow 2C_5H_{11}OH + As_2O_3 + H_2O.$$ [296]

β-Chlorovinylarsonic acid, $(CHCl{=}CH)AsO(OH)_2$, is formed by oxidizing the corresponding dichloroarsine with concentrated nitric acid. It crystallizes from acetone-carbon tetrachloride in long needles, m. p. 130°. Its monosodium salt crystallizes in hexagonal plates or long needles, m. p. 163° with decomposition. On heating the free acid at 110-15°, it loses one molecule of water forming the anhydride, $CHCl{=}CH.AsO_2$, a white, hygroscopic powder decomposing violently at 242°.[181]

3. *Alkyl Arsinedisulfides.*—Theoretically, the alkyl arsinedisulfides may be regarded as arsonic acid anhydrides with the oxygen replaced by sulfur:



Arsonic Acid Anhydride Disulfide

That there is actually an exchange of sulfur for oxygen, may be assumed from the general method of preparation which consists in passing hydrogen sulfide through aqueous solutions of the arsonic acids, the reaction proceeding according to the following equation:

$$RAsO(OH)_2 + 2H_2S \longrightarrow RAsS_2 + 3H_2O.$$

Moreover, by employing certain oxidizing agents the disulfides can be converted into the corresponding arsonic acids with the liberation of sulfur, further indicating the mutual exchangeability of the sulfur and oxygen in these two classes of arsenicals. The members of this group are yellow oils having a repulsive odor, and generally dissolve in the usual organic solvents.

Methylarsinedisulfide, CH_3AsS_2, is prepared by passing hydrogen sulfide through a solution of methylarsonic acid,[33, 297] separating slowly in the form of clear yellow oily drops which on cooling first become turbid and finally semi-solid. After washing with water and drying over calcium chloride, it is dissolved in chloroform and the latter evaporated off, the disulfide remaining as a yellow, gummy mass, which cannot be solidified. According to Meyer it is not necessary to isolate the arsonic

acid for the preparation of the disulfide, for upon heating sodium arsenite and methyl iodide together in a sealed tube, dissolving the melt in warm water, acidulating with hydrochloric acid and treating the solution with hydrogen sulfide, the above disulfide may be obtained.

The product, which may be purified by means of carbon bisulfide, has a repulsive smell, is soluble in ether, alcohol, chloroform, carbon bisulfide, or warm caustic soda solution, but difficultly so in ammonia. Dilute nitric acid oxidizes it to methylarsonic acid which may be identified by its calcium and silver salts. According to Meyer, the disulfide decomposes on heating into methyl sulfide and arsenic trisulfide:

$$2CH_3AsS_2 \longrightarrow (CH_3)_2S + As_2S_3.$$

This would resemble the observation made by Baeyer upon heating methylarsine tetrachloride[276] when methyl chloride and arsenic trichloride are produced:

$$CH_3AsCl_4 \longrightarrow CH_3Cl + AsCl_3.$$

Dehn, however, claims[298] that the disulfide when heated decomposes into trimethylarsine sulfide and arsenic pentasulfide:

$$3CH_3AsS_2 \longrightarrow (CH_3)_3AsS + As_2S_5.$$

Ethylarsinedisulfide slowly separates on passing hydrogen sulfide through a hydrochloric acid solution of magnesium ethylarsonate.[299] It is a yellow, highly viscid oil of a peculiar, disagreeable odor; sp. gr. 1.836/24°; sparingly soluble in ligroin, readily in benzene, chloroform or carbon bisulfide, and insoluble in water, alcohol or ether. Like arsenic trisulfide, methylarsinedisulfide or phenylarsinesulfide it does not dissolve in concentrated hydrochloric acid, but is readily soluble in caustic alkalis or alkali sulfides. Dilute nitric acid dissolves it, yielding ethylarsonic acid, while concentrated nitric acid acts on it with explosive violence, yielding ethylarsonic, acetic and arsenic acids.

n-Propylarsinedisulfide, similarly prepared from magnesium n-propylarsonate,[300] is a viscid oil changing to a gummy mass below — 10°. Its density is 1.8 at ordinary temperature.

Isoamylarsinedisulfide is a viscid, pale yellow oil which cannot be solidified in a freezing mixture and cannot be distilled without decomposition. It is prepared like its lower homologues.[301]

B. Secondary Derivatives.

1. *Dialkyl Arsinetrihalides,* R_2AsX_3.—Although but few of these compounds have been prepared, they are more stable than the primary alkyl tetrahalides which decompose at room temperature.

Dimethylarsinetrichloride (*Cacodyl trichloride*), $(CH_3)_2AsCl_3$, is prepared by passing chlorine into a carbon bisulfide solution of cacodyl chloride:

$$(CH_3)_2AsCl + Cl_2 \longrightarrow (CH_3)_2AsCl_3,$$

or by slowly introducing powdered cacodylic acid into phosphorus pentachloride or -oxychloride in the presence of dry ether:

$$(CH_3)_2AsO.OH + 2PCl_5 \longrightarrow (CH_3)_2AsCl_3 + 2POCl_3 + HCl.$$

The product crystallizes from ether in prisms or leaflets readily hydrolyzed by water, and decomposing at 40-50° into methyldichloroarsine and methyl chloride.[302]

Diethylarsinetrichloride.—When a dilute alcoholic solution of mercuric chloride is gradually introduced into an alcoholic solution of diethylarsine, a white precipitate forms and the whole develops an unbearable odor, which gradually disappears as more bichloride is added. By warming the mixture on a water-bath a clear solution results, which when cooled yields a white, crystalline powder. Two other compounds are formed at the same time, one settling to the bottom of the container in the form of heavy, oily drops which solidify upon cooling to a hard, brittle, amorphous, greenish-gray mass; the other separating in the form of colorless needles upon filtering off the above two substances and concentrating the filtrate. These latter two compounds have not been identified.

The above white, crystalline powder, $(C_2H_5)_2AsCl_3.4HgO$, is odorless, difficultly soluble in cold, more readily in hot water, and almost insoluble in alcohol. It is unaffected by dilute nitric acid, but is decomposed by the concentrated reagent. When heated it decomposes, forming mercuric chloride and volatile arsenical products.[303]

Diisoamylarsinechlorodibromide, $(C_5H_{11})_2AsCl.Br_2$, separates on adding bromine to a dry ethereal solution of diisoamylchloroarsine as long as decolorization occurs on gentle warming, evaporating off the solvent and permitting the residual oil to stand. It forms white crystalline granules with an odor resembling chloral hydrate; melts at 124-5°; is readily soluble in ether, chloroform or ammonia, less so in water or benzene, and is converted into diisoamylarsinic acid by aqueous ammonia.[304]

2. *Dialkyl Arsinic Acids,* $R_2AsO.OH$.—These acids constitute an important chapter of organic arsenicals chiefly because of the historical and practical importance attached to the first member of the series, dimethylarsinic- or cacodylic acid, which attracted the attention of such notable pioneers as Bunsen, Berzelius, J. B. Dumas, Frankland, Kolbe, Cahours, Landolt and von Baeyer. It is characterized by a remarkable

stability toward oxidizing agents and by its non-toxicity in the animal body.

Although Auger had prepared cacodylic acid in 1903 by Meyer's method, he was unsuccessful with the higher homologues, so that it appeared as though this method could not be employed for the synthesis of dialkyl arsinic acids in general.

In 1921, however, Quick and R. Adams succeeded in obtaining aliphatic arsinic acids by this method. They first prepared arsonic acids according to Meyer's procedure, and by reduction with sulfur dioxide in the presence of hydrochloric acid converted them into dichloroarsines. The latter were then dissolved in four moles of sodium hydroxide forming disodium alkyl arsenites, and converted into arsinic acids by treatment with alkyl halides under the same conditions as those employed in the preparation of primary arsonic acids. The reactions take place rapidly, a maximum of four hours being required to prepare the final products. Their isolation is slightly more difficult than that of the arsonic acids, due to their greater solubility in water, but precipitation is readily effected by neutralizing the reaction mixture, concentrating, filtering off inorganic salts and finally acidifying.

The activity of the halogen in alkyl halides and the solubilities of the latter are very important factors in determining the speed of reaction between alkyl chlorides or bromides and sodium arsenite or sodium alkyl arsenites. Thus, benzyl chloride, allyl bromide and ethylene chlorhydrin react from five to ten times as rapidly as ethyl- or isopropyl bromide. Moreover, with a series of alkyl halides the speed of reaction diminishes as the molecular weight increases. Aryl halides cannot be used in the above reaction.

The acids of this group may also be prepared from secondary trivalent aliphatic arsenicals by oxidation with oxygen or mercuric oxide; from alkyldichloroarsines and bromine in the presence of water, or by the action of mercuric oxide upon alkyl arsineoxides. They consist of well-defined crystalline substances soluble in water or alcohol, and are readily reduced to trivalent arsenicals by nascent hydrogen. They form metallic salts, but cacodylic acid also possesses basic properties forming salts with acids. The acids do not yield a precipitate with magnesia mixture either in the hot or cold, thereby differing from both arsenic- and the primary arsonic acids.

Dimethylarsinic (Cacodylic) acid, $(CH_3)_2AsO.OH$, is obtained in practically theoretical yields by oxidizing the corresponding arsineoxide with mercuric oxide under water, the reaction being so vigorous that it must be regulated by outside cooling. When the odor of cacodyl oxide has entirely disappeared, the supernatant fluid is poured off from the metallic mercury and cacodyl oxide added drop by drop until, on warming, metallic mercury no longer separates, thereby indicating the com-

plete decomposition of any mercury cacodylate formed. The solution is then concentrated and the product finally recrystallized from alcohol.[305]

Auger[306] prepared the same acid by further application of Meyer's reaction. Disodium methylarsonate is first reduced to methylarsineoxide by dissolving in a minimum amount of luke warm water, saturating with sulfur dioxide at ordinary temperature and boiling in a reflux apparatus. The excess of sulfur dioxide is neutralized with sodium carbonate, the whole evaporated to dryness in vacuo, and the arsineoxide removed from the residue by repeated extraction with hot benzene. The product is then dissolved in methyl alcohol, and refluxed with one mole of methyl iodide in the presence of two moles of caustic soda. When the reaction is completed, the alcohol is distilled off, and the residue treated with dilute sulfuric acid and aqueous sodium nitrite. After filtering off the liberated iodine, the filtrate is saturated with sodium carbonate, evaporated to dryness, and the sodium cacodylate extracted from the residue by means of absolute alcohol.

The free acid exists as colorless, odorless, obliquely truncated prisms melting at 200°; has a slightly acid taste; is neutral to methyl orange but acid to phenolphthalein, and readily dissolves in water or alcohol. It is a remarkably stable compound, remaining undecomposed by the action of fuming nitric acid, aqua regia or potassium permanganate even upon heating,[307] but deflagrating when heated with dry chromic acid. When electrolyzed in alkaline solution, it is oxidized to arsenic acid.[308] Cacodylic acid is also unaffected by sulfurous acid, oxalic acid, ferrous sulfate, nascent hydrogen or other milder reducing agents, but is reduced to cacodyl oxide by warming with phosphorous acid, to cacodyl chloride by stannous chloride, to cacodyl and dimethylarsine by electrolysis in 2N-sulfuric acid solution,[308] while with metallic zinc, cacodyl oxide and zinc cacodylate are formed. On passing hydrogen iodide over the dry acid, much heat is evolved, cacodyl iodide, free iodine and water being formed. Similar results are obtained with hydrobromic acid. With hydrogen chloride, methyldichloroarsine and methyl chloride are formed; with hydrogen sulfide, cacodyl sulfide, sulfur and water result, while with phosphorus pentachloride, cacodyl trichloride is obtained.

It is amphoteric, forming salts with bases and also acids, e. g., $(CH_3)_2AsO_2H.HCl$, $(CH_3)_2AsO_2Na$. According to Hantzsch, conductivity measurements with cacodylic acid show that when treated with an excess of caustic alkali, it does not react strictly as a monobasic acid, but partly as the sodium salt of a tribasic acid. He concluded that in the presence of one molecule of sodium hydroxide the acid is monobasic, but with an excess of alkali it forms the molecular aggregate $(CH_3)_2As(OH)(ONa)_2$, so that the acid is capable of functioning in the tribasic form, $(CH_3)_2As(OH)_3$. This effect is very slight, however, and disappears entirely in $\frac{N}{48}$ solution.[309]

At 120° the acid reacts with easily meltable condensation products of phenols and formaldehyde, forming resinous substances in which the arsenic is held in an ester-like combination. These form water-soluble salts with alkalis, and are soluble in the same solvents as the parent phenolic condensation compounds, upon which their melting points are also dependent.[310]

Salts.—With potassium or sodium hydroxides the acid forms deliquescent salts, of which the sodium compound is the more stable. The silver salt, prepared by dissolving pure silver oxide or carbonate in cacodylic acid, crystallizes in long needles readily soluble in water and darkening in sunlight. It combines with the free acid, forming a salt, $(CH_3)_2AsO_2Ag.2(CH_3)_2AsO_2H$, and also with silver nitrate, forming the compound, $(CH_3)_2AsO_2Ag.AgNO_3$—scales readily soluble in water, sparingly in alcohol.[311] Mercuric cacodylate is obtained almost pure by dissolving freshly precipitated mercuric oxide in an excess of a concentrated solution of the acid. It crystallizes in fine white needles which when heated yield metallic mercury and a mixture of volatile products having an odor like "Alkarsin."[312] The copper salt, $[(CH_3)_2AsO.O]_2Cu.7CuCl_2$, results upon mixing alcoholic solutions of cacodylic acid and copper chloride, a slimy, greenish sediment being formed at first which becomes granular on boiling. It is soluble in water, and decomposes when heated, yielding cacodyl, copper chloride, copper arsenite, arsenic and carbon.[313] In addition, there have been prepared lithium, calcium, barium, magnesium, iron, strychnine, codeine and antipyrine salts.

Rare Earth Cacodylates.—Praseodymium cacodylate, $[(CH_3)_2AsO_2]_6Pr_2.16H_2O$, prepared by dissolving praseodymium hydroxide in a boiling solution of cacodylic acid, forms pale green crystals soluble in water.[314] Neodymium cacodylate is similarly obtained as small crystals of a very pale amethyst color and soluble in water. Samarium cacodylate forms almost white crystals very soluble in boiling water, much less in cold, and insoluble in alcohol or acetone.[314, 315] Yttrium cacodylate is precipitated by boiling a neutral solution of yttrium chloride with a slight excess of sodium cacodylate, and consists of small white crystals very slightly soluble in boiling water and insoluble in cold. Thulium cacodylate, prepared like the praseodymium salt, is a crystalline powder practically insoluble in boiling water.

Perhaps the most remarkable property of the above compounds is the ease with which they form double salts with rare earth chlorides, nitrates, sulfates, etc. Thus, double salts of lanthanum cacodylate and lanthanum chloride, -bromide, -iodide, -nitrate, -sulfate and -methanetrisulfonate have been prepared. Cerium chloride cacodylate, $2Ce[(CH_3)_2AsO_2]_3.CeCl_3.18H_2O$, consists of white fibrous crystals;

cerium sulfate cacodylate is obtained as a thick precipitate by mixing the sulfate and cacodylate solutions, while neodymium chloride cacodylate forms very pale amethyst crystals of a fibrous nature.[314]

The hydrochloride, $(CH_3)_2AsO_2H.HCl$, prepared by the direct combination of its components, crystallizes in leaflets which are readily decomposed into their constituents by means of water. The corresponding hydrobromide is a very unstable syrupy mass, while the hydrofluoride is supposed to correspond to the formula, $[(CH_3)_2AsO_2H.HF](CH_3)_2AsF_3$. On treating monosodium cacodylate with four moles of molybdenum trioxide in boiling water, a sodium salt, $Na_2H\left[\begin{matrix}(CH_3)_2\\ As(Mo_2O_7)_2\\ (OH)_2\end{matrix}\right]$, is obtained, which when treated with an excess of guanidinium chloride yields colorless plates of a compound, $(CN_3H_6)_2H\left[\begin{matrix}(CH_3)_2\\ As(Mo_2O_7)_2\\ (OH)_2\end{matrix}\right]$. The corresponding potassium, silver, copper and lead salts have also been prepared.[316] The thiosinamine salt, $S=C<\begin{matrix}NH.C_3H_5\\ NH_2\end{matrix}.(CH_3)_2AsO_2H$, prepared from its components, is a crystalline compound, m. p. 74°; readily soluble in water or alcohol, less so in ether, and difficultly in ligroin or benzene.[317]

Diethylarsinic acid, $(C_2H_5)_2AsO.OH$, is prepared by oxidizing an alcoholic solution of ethylcacodyl with oxygen, or treating ethylcacodyl with finely ground mercuric oxide under water and isolating through the barium salt.[318]

Another method consists in permitting ethyl bromide to react with ethyl dichloroarsine in alkaline solution.[319] It forms lustrous, deliquescent leaflets melting at 190° and decomposing at higher temperature, yielding arsenic acid and other arsenical decomposition products. When heated in air it burns with a pale yellow flame. It is readily soluble in water or alcohol, sparingly in ether; has an acid reaction; and a taste which is at first acid and finally bitter. It decomposes alkali carbonates, liberating carbon dioxide. The acid is a very stable substance, remaining unaffected by oxidizing agents such as concentrated nitric acid or aqua regia, and by weak reducing agents like sulfurous acid or ferrous sulfate. Phosphorous acid reduces it upon warming, yielding an oily liquid with a penetrating odor, probably diethylarsineoxide. Its barium salt, $[(C_2H_5)_2AsO_2]_2Ba.(C_2H_5)_2AsO_2H.2H_2O$, is a deliquescent, crystalline substance easily soluble in water, less so in alcohol, and decomposing when heated. The silver salt is a very unstable substance darkening readily at ordinary temperature, more so upon warming. When dry it is a black amorphous powder unaffected by dilute hydrochloric acid, but soluble in the concentrated acid with decomposition. On account

of its instability Landolt was unable to determine the exact composition of the silver salt, the analyses for silver varying from 28.6 to 56.7 per cent. With ferric chloride diethylarsinic acid yields a brown precipitate difficultly soluble in hydrochloric acid; with lead acetate a white precipitate; with cupric sulfate a pale green precipitate, and with mercurous nitrate a white precipitate insoluble in dilute nitric acid. The mercuric salt is a deliquescent, crystalline substance.

Di-n-propylarsinic acid, $(C_3H_7)_2AsO.OH$, prepared by distilling tetra-n-propylarsonium hydroxide in vacuo,[320] forms lustrous leaflets or needles, m. p. 123°.

n-Propyl-n-butylarsinic acid, $(C_3H_7)(C_4H_9)AsO.OH$, from n-propyl bromide and n-butyldichloroarsine in alkaline solution, melts at 127-8°.[172]

Di-n-butylarsinic acid, $(C_4H_9)_2AsO.OH$, similarly prepared from n-butyl bromide and n-butyldichloroarsine, melts at 137-8°. Its cupric salt is a pale blue precipitate obtained by adding copper sulfate solution to a neutral solution of the acid.[172]

Diisoamylarsinic acid, $(C_5H_{11})_2AsO.OH.2H_2O$, is obtained together with arsenic- and isoamylarsonic acids upon warming basic diisoamylchloroarsine with bromine water and dissolving the resulting yellow, crystalline solid in ammonium hydroxide. The arsenic acid is first precipitated in the cold by the addition of an excess of magnesium chloride, while upon boiling the filtrate, a precipitate of magnesium isoamylarsonate is obtained. The free diisoamylarsinic acid is then isolated from the final filtrate by acidulating. It may also be prepared by treating diisoamylarsinechlorodibromide with water or aqueous ammonia. The product crystallizes from water in large, flaky crystals m. p. 153-4°; easily soluble in alcohol, less so in water and insoluble in ether.[239]

Symm. Tetraiodocacodylic acid [Bis(diiodomethyl)arsinic acid], $(CHI_2)_2AsO.OH$, the preparation of which has been previously described under diiodomethylarsonic acid, consists of small yellow crystals insoluble in water, but soluble in hot acetic or nitric acid. Continued boiling with the latter decomposes it into arsenic acid, iodine and carbon dioxide. It is also decomposed by hot alkali:

$$(CHI_2)_2AsO.OH + 2NaOH \longrightarrow 2CH_2I_2 + Na_2HAsO_4.$$

The sodium salt, obtained by neutralizing the acid with sodium carbonate, crystallizes from water-alcohol solution in well-defined yellowish crystals containing $6H_2O$, and very soluble in water.[287]

Di(β-chlorovinyl)arsinic acid, $(CHCl{=}CH)_2AsO.OH$.—Upon oxidizing the corresponding chloroarsine with nitric acid, and recrystallizing

the resulting product from chlorofrom, needle-shaped crystals of the nitrate, $(CHCl=CH)_2AsO_2H.HNO_3$, m. p. 99°, are obtained. The free acid is produced by hydrolyzing the salt with water and alcohol containing enough caustic soda to neutralize the liberated nitric acid, and removing the arsinic acid with chloroform. It crystallizes in colorless needles, m. p. 120°. The potassium salt, containing $4H_2O$, forms colorless plates, m. p. 49°. The anhydrous variety is a white, hygroscopic powder, m. p. 158° with decomposition. The sodium salt crystallizes in colorless plates containing $4H_2O$ and melting at 70°.[321]

Thiocacodylic acid, $(CH_3)_2AsS.SH$, is not known in the free state. Upon attempting to replace the oxygen of cacodylic acid with sulfur by means of hydrogen sulfide in aqueous or alcoholic solution, there are obtained cacodyl mono- and disulfides respectively. The lead, cuprous, bismuth, antimony and aurous thiocacodylates, however, have been prepared by the action of hydrogen sulfide upon the respective cacodylates,[322] or from cacodyl disulfide and metallic salts in alcoholic medium.

Aurous thiocacodylate, $(CH_3)_2AsS.SAu$, is a yellowish powder insoluble in water, alcohol, ether or hydrochloric acid. It is decomposed by fuming nitric acid with the separation of gold and sulfur, while with potassium hydroxide gold sulfide is obtained. When heated alone, it decomposes into cacodyl sulfide, gold and sulfur. The cuprous salt is a yellow powder insoluble in water, acids, alkalis or the usual organic solvents, and when heated, decomposes into cacodyl sulfide, sulfur and copper sulfide. The bismuth salt forms golden-yellow, insoluble flakes unaffected below 100°, but decomposing at higher temperatures into sulfur, bismuth- and cacodyl sulfides, while the lead salt consists of stable, white scales sparingly soluble in alcohol.

C. Tertiary Derivatives.

1. *Trialkylarsine Dihalides, Hydroxyhalides and Cyanohalides,* R_3AsX_2, $R_3As.OH.X$, $R_3As.CN.X$.—Like the primary arsinetetrahalides and secondary arsinetrihalides, the trialkylarsine dihalides are unstable compounds easily hydrolyzed by atmospheric moisture and difficult to preserve in the pure state. They may be prepared:

1. By the action of haloid acids upon trialkylarsine oxides:

$$R_3AsO + 2HX \longrightarrow R_3AsX_2 + H_2O.$$

2. From trialkylarsine sulfides and haloid acids:

$$R_3AsS + 2HX \longrightarrow R_3AsX_2 + H_2S.$$

3. On combining trialkylarsines with halogens:

$$R_3As + X_2 \longrightarrow R_3AsX_2.$$

4. By the action of Grignard's reagent upon arsenic trihalides.

The products are solids which generally dissolve in water with hydrolysis. When distilled they decompose into a dialkyl halogenated arsine and an alkyl halide:

$$R_3AsX_2 \longrightarrow R_2AsX + RX.$$

Tertiary arsines combines with cyanogen bromide in an atmosphere free of moisture, forming trialkyl cyanobromides:

$$R_3As + CN.Br \longrightarrow R_3As.CN.Br.$$

The latter are extremely sensitive to moisture, the cyanogen group being replaced by a hydroxyl with the formation of the corresponding hydroxybromide:

$$R_3As.CN.Br + H_2O \longrightarrow R_3As.OH.Br + HCN.$$

Trimethylarsine dibromide, $(CH_3)_3AsBr_2$.—Upon adding an excess of bromine to an ethereal solution of trimethylarsine, a red precipitate of trimethylarsinetetrabromide, $(CH_3)_3AsBr_4$, is formed, which is converted into the dibromide by treatment with acetone.[323] It may also be prepared by heating together cacodyl bromide and methyl bromide in a sealed tube filled with dry carbon dioxide for three hours in a boiling water-bath.[211] It is a colorless crystalline substance melting between 150 and 160°, and dissolving in water with hydrolysis.

Trimethylarsine diiodide is prepared from trimethylarsine and iodine.[324] Upon distillation it decomposes into dimethyliodoarsine and methyl iodide:

$$(CH_3)_3AsI_2 \longrightarrow (CH_3)_2AsI + CH_3I.$$

Triethylarsine dichloride.—Landolt obtained traces of this compound by treating triethylarsine oxide with concentrated hydrochloric acid in alcoholic solution.[325] By the action of mercuric chloride upon triethylarsine he obtained needles of $(C_2H_5)_3AsO.(C_2H_5)_3Cl_2.Hg_2Cl_2$.[326] An attempt to prepare the dichloride by decomposing the corresponding diiodide with mercuric chloride proved unsuccessful.

Triethylarsine dibromide, $(C_2H_5)_3AsBr_2$, is prepared by adding bromine to triethylarsine in alcoholic solution,[327] or by the action of concentrated hydrobromic acid upon triethylarsine sulfide.[328] According to Landolt it is a pale yellow, crystalline mass, but Dehn obtained it in practically white, deliquescent needles with a bitter taste and an irritating odor. When treated with chlorine or nitric acid, bromine is liberated, while with concentrated sulfuric acid hydrobromic acid is obtained. Upon heating it melts and finally burns with a white flame.

Triethylarsine diiodide.—Prepared from triethylarsine and iodine in ethereal solution,[329] or by distilling the compound $(C_2H_5)_4AsI.AsI_3$.[330] It consists of sulfur-yellow flakes melting at 160° and boiling at 190.° It is very unstable; exposed to the air for a short time it turns brown and melts to a dark syrupy liquid. The compound is readily soluble in water, alcohol or warm hydrochloric acid, sparingly so in ether, and is decomposed by nitric or sulfuric acid with separation of iodine. Aqueous caustic potash converts it into the corresponding arsine oxide.

Dimethylallylarsine dibromide, $(CH_3)_2(C_3H_5)AsBr_2$, is obtained as a yellow flocculent precipitate by treating dimethylallylarsine with bromine in ether solution.[331]

Tri(β-chlorovinyl)arsine dibromide, $(CHCl=CH)_3AsBr_2$, from the tertiary arsine and bromine in light petroleum solution at freezing temperature, consists of colorless needles melting at 107°.[332]

Triethylarsine hydroxybromide, $(C_2H_5)_3As.OH.Br$.—When a dry ethereal solution of triethylarsine (1:10) is slowly treated with a similar solution of an equimolecular amount of dry cyanogen bromide at low temperature, a white, crystalline hydroxybromide separates out. In this reaction the cyanobromide is first formed, but is immediately hydrolyzed by atmospheric moisture. It crystallizes from acetone in needles, m. p. 149-50°; readily soluble in water with an acid reaction, also in alcohol, chloroform, glacial acetic acid, phenol or warm acetone, and insoluble in ether, ligroin or carbon bisulfide.[333]

Ethyldi-n-propylarsine hydroxybromide, $(C_2H_5)(C_3H_7)_2As.OH.Br$, is prepared by dissolving the corresponding cyanobromide in a little alcohol and concentrating in vacuo. It exists as crystals which are so hygroscopic that they melt immediately on coming in contact with air. It forms a *hydroxypicrate,* m. p. 85.5°, with picric acid in alcoholic solution.[269]

Ethyldiisobutylarsine hydroxybromide, $(C_2H_5)(C_4H_9)_2As.OH.Br$, is made either by allowing atmospheric moisture to act on the cyanobromide, or by bringing together ethyldiisobutylarsine and cyanogen bromide in moist ether. It exists in a liquid or salve-like form. Its *hydroxypicrate* crystallizes in fine, yellow needles melting at 82°.[226]

Triethylarsine cyanobromide, $(C_2H_5)_3As.CN.Br$.—Triethylarsine dissolved in absolute petroleum ether is mixed with a similar solution of one molecular equivalent of anhydrous cyanogen bromide in an atmosphere of carbon dioxide which has been dried by passing successively through calcium chloride, sulfuric acid and phosphorous pentoxide. After standing for some time, crystals of the cyanobromide separate out. It melts at 67°, and absorbs moisture with great avidity, the

hydroxybromide being formed.[334] Distilled in vacuo, it decomposes, yielding diethylcyanoarsine and ethyl bromide:

$$(C_2H_5)_3As.CN.Br \longrightarrow (C_2H_5)_2As.CN + C_2H_5Br.$$

Ethyldi-n-propylarsine cyanobromide, $(C_2H_5)(C_3H_7)_2As.CN.Br$, from the corresponding tertiary arsine and cyanogen bromide like the preceding compound, is a granular substance very sensitive to moisture. When heated under special conditions, it breaks up into a mixture of ethyl- and n-propyl bromides on the one hand and a mixture of ethyl-n-propyl- and di-n-propylcyanoarsines on the other.[268]

Ethyldiisobutylarsine cyanobromide, $(C_2H_5)(C_4H_9)_2As.CN.Br$, similarly prepared, is a solid melting at 69°. On heating it decomposes into ethyl bromide and diisobutylcyanoarsine.[226]

2. *Trialkylarsine Oxides.*—This class of compounds may be regarded as having been derived from ortho arsenic acid by replacing its hydroxyl groups with alkyl radicals:

$$OAs\begin{cases}OH\\OH\\OH\end{cases} \longrightarrow OAs\begin{cases}R\\R.\\R\end{cases}$$

They result when tertiary arsines are exposed to the action of the air. Unlike the arsonic and arsinic acids the trialkylarsine oxides possess no acid properties. They have a neutral reaction toward litmus, but possess feebly basic properties. Thus, the trimethyl, triethyl and tri(β-chlorovinyl) derivatives form nitrates with nitric acid.

Trimethylarsine oxide, $(CH_3)_3AsO$, is obtained as colorless deliquescent crystals, when trimethylarsine is exposed to the air,[335] or from cacodyl oxide by Meyer's reaction:

$$[(CH_3)_2As]_2O + 2CH_3I + 2NaOH \longrightarrow 2(CH_3)_3AsO + 2NaI + H_2O.$$ [336]

With molybdenum trioxide in boiling water, it forms a yellowish microcrystalline powder consisting of

$$As(CH_3)_3(OH)_3H_3\left[\begin{matrix}(CH_3)_3 & & (CH_3)_3\\ As(Mo_2O_7)_2 & & (Mo_2O_7)_2As\\ & -O- & \end{matrix}\right].3H_2O.$$

If guanidinium chloride be added to the solution before the above compound crystallizes out, there are finally obtained white, microcrystalline platelets of a compound, $(CN_3H_6)_3H_3\left[\begin{matrix}(CH_3)_3 & & (CH_3)_3\\ As(Mo_2O_7)_2 & & (Mo_2O_7)_2As\\ & -O- & \end{matrix}\right]$.[337]

Triethylarsine oxide, $(C_2H_5)_3AsO$.—When an ethereal solution of triethylarsine is allowed to evaporate spontaneously in the air at ordinary temperature, the oxide is obtained as a colorless, oily liquid with a faint garlicky odor. It is contaminated with other oxidation products, the nature of which has not been further investigated. It can be prepared in larger quantities by the action of ethyl iodide on sodium arsenide. In this method the product is first extracted with ether, then with alcohol, the solvent evaporated off from the latter extract and the residual liquid distilled. The oxide is a faint yellow, oily liquid insoluble in water, hydrochloric or sulfuric acid, soluble in ether or alcohol.[338] It dissolves in nitric acid, forming a nitrate which can also be prepared from triethylarsine and nitric acid.

Tri-n-propylarsine oxide, $(C_3H_7)_3AsO$, is obtained by the dry distillation of tetra-n-propylarsonium hydroxide. Its mercurichloride, $(C_3H_7)_3AsO \cdot 2HgCl_2$, consists of white needles, m. p. 60-60.5°.[339]

Tri(β-chlorovinyl)arsine oxide, $(CHCl{=}CH)_3AsO$, is formed by treating an aqueous solution of the corresponding hydroxynitrate with the proper quantity of sodium hydroxide and extracting with chloroform. It is also formed on treating the corresponding dibromide with caustic soda. It crystallizes in long, colorless needles or small plates, m. p. 154° with decomposition.[332]

3. *Trialkylarsine Sulfides,* R_3AsS.—The arsenicals included in this group are analogous to those of the preceding chapter, as they are formed from trialkylarsines by direct combination with sulfur. They also result when the corresponding arsine oxides are treated with hydrogen sulfide. This conversion of oxygen compounds into the corresponding sulfur derivatives is accomplished more easily than that of the primary or secondary arsenicals.

A very interesting method of preparation has been employed by Dehn. It consists in heating an alkyl arsinedisulfide to a high temperature, a tertiary alkylarsine sulfide being formed together with arsenic pentasulfide:

$$3RAsS_2 \longrightarrow R_3AsS + As_2S_5.$$

Thus it can be seen that the above tertiary compounds are very stable, a fact which Landolt had previously pointed out.

Trimethylarsine sulfide, $(CH_3)_3AsS$, may be prepared by combining trimethylarsine with sulfur;[340] by dissolving trimethylarsine dibromide in absolute alcohol, converting into the oxide by means of two moles of potassium ethylate, and treating this with hydrogen sulfide;[341] or by heating methylarsinedisulfide:

$$3CH_3AsS_2 \longrightarrow (CH_3)_3AsS + As_2S_5.^{298}$$

It forms colorless prisms or needles soluble in alcohol, chloroform or carbon bisulfide, m. p. 168° (Hantzsch), 174° (Dehn), 177.5° (Dehn, Wilcox).[342] With methyl iodide it forms an additive compound, $(CH_3)_3As<\begin{matrix}S.CH_3\\I\end{matrix}$ or $(CH_3)_3AsS<\begin{matrix}CH_3\\I\end{matrix}$, which crystallizes from hot alcohol in white needles melting with decomposition at 180° and decomposed by water, yielding methyl mercaptan.[341]

Triethylarsine sulfide, $(C_2H_5)_3AsS$, is derived from triethylarsine and flowers of sulfur in ether medium. The product thus obtained is contaminated with sulfur and triethylarsine oxide.[343] It may also be prepared by heating ethylarsinedisulfide at 180-95°;[298] by boiling triethylarsine oxide with aqueous potassium pentasulfide;[291] or from triethylarsine by heating with four parts of carbon bisulfide and three parts of absolute alcohol in a sealed tube at 120° for 10 hours, evaporating off the excess of carbon bisulfide and alcohol, and fractionating the residual oil. The fraction obtained above 200°, on standing for a number of days, deposits the above sulfide as long needles. At present no equation can be given that will represent this peculiar reaction.[344]

The sulfide consists of feathery crystals or white needles with a bitter taste; soluble in warm water, boiling ether or alcohol; melts at 119.5°; and sublimes at higher temperatures. According to Landolt it is odorless, while Dehn found that it possesses a very peculiar, penetrating and disagreeable odor. It is decomposed by concentrated nitric acid, the sulfur being oxidized to sulfuric acid, but is unaffected by boiling with caustic potash.

Trimethylarsine selenide, $(CH_3)_3AsSe$, formed from the tertiary arsine and powdered selenium in ethereal solution, crystallizes in long, thin needles unstable in air, giving off an odor similar to that of trimethylarsine, and rapidly forming a brick-red deposit on the surface. This reddish substance is somewhat soluble in alcohol or carbon bisulfide, and is probably amorphous selenium. The above crystals are fairly stable when covered with alcohol or ether or when dissolved in water, especially if kept in the dark. On exposure to light, however, the reddening occurs even when covered with alcohol. Upon heating, the compound begins to decompose appreciably at 100°, evolving vapors which are probably those of trimethylarsine, and finally leaving a black residue of selenium.[345]

D. Quaternary Derivatives.

1. *Tetraalkyl Arsonium Compounds,* R_4AsX.—Landolt, in 1854,[346] was practically the first to prepare a compound of this type. By the interaction of sodium arsenide and ethyl iodide, he obtained a mixture of several arsenicals, from which he succeeded in isolating triethylarsine.

He found that this compound could be combined additively with ethyl iodide forming a product which we now know as tetraethylarsonium iodide. He also noted that the iodine of the latter could be replaced by a hydroxyl upon treatment with moist silver oxide:

$$2(C_2H_5)_4AsI + Ag_2O + H_2O \longrightarrow 2(C_2H_5)_4As.OH + 2AgI.$$

Cahours and Riche [15] repeated Landolt's experiments with sodium arsenide using methyl- instead of ethyl iodide, and obtained principally tetramethylarsonium iodide along with small amounts of cacodyl and trimethylarsine. They also prepared the arsonium hydroxide from the iodide by means of silver oxide. The same investigators later modified the preparation of arsonium compounds by heating alkyl iodides with metallic arsenic in sealed tubes at 160-75° for 20 to 24 hours, obtaining double compounds of the arsonium iodide and arsenic triiodide:

$$4RI + 2As \longrightarrow R_4AsI.AsI_3.$$

By boiling with concentrated potassium hydroxide solution these were decomposed into the arsonium compound, potassium iodide, potassium arsenite and water, while upon distillation with solid caustic potash, trimethylarsine resulted.[347] By employing zinc- or cadmium arsenide instead of metallic arsenic they obtained double compounds of the formula $R_4AsI.ZnI_2$ or $-CdI_2$ respectively, which upon boiling with concentrated caustic potash solution yielded the arsonium iodide, a metallic oxide and potassium iodide.[348]

The arsonium iodides have also been obtained from primary arsines by heating with an excess of alkyl iodide:

$$RAsH_2 + 3R'I \longrightarrow RR'_3AsI + 2HI.$$

In 1897-98 Partheil and Amort prepared a mercuric arsenide, Hg_3As_2, by the action of arsine upon mercuric chloride: [349]

$$2AsH_3 + 3HgCl_2 \longrightarrow As_2Hg_3 + 6HCl.$$

Upon heating this substance with alkyl iodides in a sealed tube they claimed that double salts of hexaalkyldiarsonium iodides and mercuric iodide were formed, which with moist silver oxide yielded the free hexaalkyldiarsonium hydroxides:

$$Hg_3As_2 + 6RI \longrightarrow \left[\begin{array}{ccc} R_3As & - & AsR_3 \\ \vdots & & \vdots \\ I & & I \end{array}\right].2HgI_2 + Hg$$

$$R_6As_2I_2.2HgI_2 + 3Ag_2O + H_2O \longrightarrow R_6As_2(OH)_2 + 6AgI + 2HgO.^{320}$$

Mannheim [350] repeated Partheil's experiments and found that the products obtained were double salts of tetraalkylarsonium iodides and mercuric iodide and suggested that the so-called "hexaalkyldiarsonium compounds" be eliminated from the list of organic arsenic compounds.

The tetraalkylarsonium compounds are analogous to the corresponding ammonium and phosphonium derivatives. Although the arsenic atom in the pentavalent form is negative, its combination with four alkyl groups constitutes a positive univalent radical, forming salts with halogens. The halides, of which the iodides crystallize best, are not decomposed by aqueous caustic potash—only upon distillation with the solid alkali does decomposition occur, the corresponding tertiary arsine resulting. The halogen may be replaced by various acid radicals by treatment with silver salts, silver halide being precipitated, e. g.,

$$R_4AsI + AgNO_3 \longrightarrow R_4As.NO_3 + AgI.$$

With moist silver oxide they yield arsonium hydroxides—strong bases absorbing moisture and carbon dioxide from the air, and forming well defined, crystalline salts with acids. The arsonium chlorides form double salts with platinic-, auric- or mercuric chloride, while the arsonium iodides combine with iodine, forming triiodides:

$$R_4AsI + I_2 \longrightarrow R_4AsI_3.$$

Tetramethylarsonium iodide, $(CH_3)_4AsI$, may be produced directly from trimethylarsine and methyl iodide. It is the chief product formed by the interaction of sodium arsenide and methyl iodide,[351] or when mercuric arsenide and methyl iodide are heated at 120°.[352] In the last method it is obtained as the double salt $(CH_3)_4AsI.HgI_2$. Other methods of preparation consist in heating methyl iodide with finely powdered arsenic in a sealed tube at 160-75° for 20-24 hours,[353] or with zinc- or cadmium arsenide at 175-80°, forming the double salts $(CH_3)_4AsI.AsI_3$, $(CH_3)_4AsI.ZnI_2$ and $(CH_3)_4AsI.CdI_2$ respectively, from which the arsonium iodide is liberated by warming with concentrated aqueous potassium hydroxide.[354] The same arsonium compound results on heating methyl iodide with methyl arsine in a sealed tube at 110° for eight hours:

$$CH_3AsH_2 + 3CH_3I \longrightarrow (CH_3)_4AsI + 2HI.$$ [355]

Finally, it may be made from cacodyl and two moles of methyl iodide:[356, 247]

$$[(CH_3)_2As]_2 + 2CH_3I \longrightarrow (CH_3)_4AsI + (CH_3)_2AsI.$$

With five molecular proportions of methyl iodide a mixture of tetramethylarsonium iodide and -triiodide is obtained which may be separated by acetone, the triiodide alone dissolving. From the latter the monciodide may be obtained by warming with concentrated caustic potash solution.

The arsonium iodide crystallizes from alcohol in cubical crystals or lustrous leaflets decomposing at 170-80°, but melting according to

Steinkopf at 328° with violent decomposition. It is readily soluble in water or alcohol, insoluble in ether, and decomposes with the formation of trimethylarsine when distilled over solid potassium hydroxide. It combines additively with iodine, forming lustrous, brown needles of the triiodide, which upon heating decomposes into methyl iodide and cacodyl iodide.

The mercuriiodide, $(CH_3)_4AsI.HgI_2$, prepared either from mercuric arsenide and methyl iodide at 120°,[352] or from tetramethylarsonium iodide and mercuric iodide in alcoholic solution,[357] crystallizes from hot alcohol in yellow needles, m. p. 184°, soluble in acetone or hot alcohol and insoluble in ether.

With iodoform in absolute alcoholic solution the arsonium iodide forms an addition product, $I[(CH_3)_4As]\ldots I_3CH$, which can also be obtained by decolorizing a hot saturated alcoholic solution of tetramethylarsonium triiodide with alcoholic potash, and recrystallizing the resulting precipitate from alcohol. The product melts at 165°; is easily soluble in hot alcohol or acetone but insoluble in cold water, ether or ligroin.[358]

Tetramethylarsonium bromide is a highly deliquescent substance produced together with cacodyl bromide from cacodyl and methyl bromide: [356]

$$[(CH_3)_2As]_2 + 2CH_3Br \longrightarrow (CH_3)_4AsBr + (CH_3)_2AsBr.$$

According to Steinkopf,[247] however, on heating the above components in a current of carbon dioxide at 100° for three hours, a mixture of the arsonium bromide and trimethylarsine hydroxybromide is obtained. The *arsonium chloride* is derived from the corresponding hydroxide and hydrochloric acid. Its mercurichloride separates from alcohol in white needles, m. p. 175-6°; sparingly soluble in cold, readily so in hot water; [359] the platinichloride, $[(CH_3)_4AsCl]_2.PtCl_4$, forms yellow crystals decomposing at 250-60°; sparingly soluble in cold, readily in hot water,[360] while the aurichloride, $(CH_3)_4AsCl.AuCl_3$, consists of yellow needles which do not melt up to 233°, are readily soluble in acetone or alcohol and insoluble in ether.[361]

Tetramethylarsonium hydroxide, $(CH_3)_4As.OH$, is obtained from the iodide by the action of moist silver oxide. It is a deliquescent, crystalline, strongly caustic substance resembling sodium- or potassium hydroxide—it forms salts with acids, even carbonic; turns red litmus blue; precipitates hydroxides of heavy metals from their soluble salts, and saponifies fats.[351]

Tetramethylarsonium triiodide, $(CH_3)_4AsI_3$, may be derived from cacodyl halides by heating with methyl iodide in a sealed tube at

100°,[200, 204, 211] or from cacodyl and five molecular proportions of methyl iodide.[247] In the last method the corresponding *arsonium iodide* is also formed, but separation is effected by acetone, in which the latter is insoluble. The triiodide crystallizes in brownish-red needles melting at 133° and yielding the monoiodide on warming with concentrated potassium hydroxide solution.

Tetraethylarsonium iodide, $(C_2H_5)_4AsI$, is prepared from triethylarsine and ethyl iodide,[346] or like the methyl compound from powdered arsenic, zinc- or cadmium arsenide and ethyl iodide.[362] It forms colorless prisms decomposing at 160°, readily soluble in water or alcohol and insoluble in ether. With silver sulfate in the presence of sulfuric acid it forms the acid sulfate, $(C_2H_5)_4As.HSO_4$.

The mercuriiodide, $(C_2H_5)_4AsI.HgI_2$, prepared like the corresponding tetramethyl compound, crystallizes from alcohol in yellow needles readily soluble in acetone, sparingly in cold alcohol, insoluble in water or ether, and melting at 112°.[363] The bismuthiiodide, $[(C_2H_5)_4AsI]_3 2BiI_3$, is formed from the arsonium triiodide by treatment with the double iodide of bismuth and potassium, $2BiI_3.3KI$. It separates as lustrous, brick-red, hexagonal plates insoluble in cold alcohol, ether or water, soluble in warm aqueous potassium iodide or hydrochloric acid, and decomposed by alkali hydroxides or carbonates.[364]

Tetraethylarsonium bromide, from the hydroxide and hydrobromic acid, consists of deliquescent crystals soluble in water or alcohol, and behaves like potassium bromide with solutions of metallic salts, nitric or sulfuric acid.[365] Its double salt with bismuth bromide, $[(C_2H_5)_4AsBr]_3.2BiBr_3$, is obtained from the arsonium triiodide by the addition of a solution of hydrated bismuth oxide in concentrated hydrobromic acid, separating as lemon-yellow crystals which decompose upon warming with alkali hydroxides or carbonates.[366]

The *arsonium chloride* results on treating the hydroxide with hydrochloric acid, and consists of deliquescent crystals readily forming double salts with metallic chlorides.[367] Its mercurichloride consists of white needles melting at 139° and dissolving in hot water; the platinichloride forms sparingly soluble, orange-yellow crystals, m. p. 224° with decomposition; the aurichloride crystallizes in yellow needles melting at 171°, and dissolving in alcohol;[368] the bismuthichloride forms colorless crystals.[369]

The *arsonium hydroxide* is obtained from the iodide by treatment with moist silver oxide. It is a highly caustic, white, deliquescent mass absorbing carbon dioxide from the air, liberating ammonia from ammonium salts, and precipitating the hydroxides of heavy metals from solutions of their salts.[346]

The *triiodide,* from the monoiodide and iodine in alcoholic solution,

consists of brown, lustrous leaflets, m. p. 55-6°; soluble in ethyl alcohol, sparingly so in ether and insoluble in carbon bisulfide. With mercury it forms the mercuriiodide, $(C_2H_5)_4AsI.HgI_2$.[370]

Tetra-n-propylarsonium iodide, $(C_3H_7)_4AsI$, is prepared from arsenic and n-propyl iodide by heating at 180° for 24-30 hours, and decomposing the resulting double iodide, $(C_3H_7)_4AsI.AsI_3$, by boiling with concentrated caustic potash solution. It crystallizes from water in white needles decomposing at 150°, readily soluble in water or alcohol and insoluble in anhydrous ether.[371] Its mercuriiodide, from the arsonium iodide and mercuric iodide, or from mercuric arsenide and n-propyl iodide at 180°, forms needles melting at 120°, soluble in acetone, sparingly so in cold alcohol, insoluble in water or ether, and yields the corresponding mercurichloride, $(C_3H_7)_4AsI.HgCl_2$, with freshly prepared silver chloride.[372]

The corresponding *arsonium chloride* is derived from the hydroxide by neutralizing with hydrochloric acid. Its mercurichloride exists as white needles, m. p. 169°; the platinichloride as yellowish-red crystals melting at 189°, while the aurichloride crystallizes in needles melting at 127°.[373]

The *arsonium hydroxide* has been obtained in impure form from the corresponding iodide or its mercuriiodide and moist silver oxide. When distilled it decomposes, yielding principally tri-n-propylarsine oxide.[374]

Tetraisopropylarsonium iodide, prepared like the normal compound from arsenic and isopropyl iodide, crystallizes in colorless needles darkening at 150°, readily soluble in alcohol and insoluble in ether.[375] Its mercuriiodide consists of yellow needles, m. p. 114°; insoluble in water or ether but soluble in acetone. The *arsonium hydroxide,* obtained in the usual manner from the iodide, reacts with hydrochloric acid yielding the corresponding *chloride.*[376] The latter forms a mercurichloride which crystallizes in needles soluble in acetone or hot water, and melting at 171°; its platinichloride decomposes at 211°, while the aurichloride, m. p. 186-8°, decomposes on exposure to light.[377]

Tetraallylarsonium iodide mercuriiodide, $(C_3H_5)_4AsI.HgI_2$, from mercuric arsenide and allyl iodide at water-bath temperature, crystallizes in yellow leaflets or plates, m. p. 74°; sparingly soluble in alcohol, readily in acetone. With freshly prepared silver chloride the double salt, $(C_3H_5)_4AsI.HgCl_2$, m. p. 72.5°, results.[378] Other allylarsonium compounds, such as the hydroxide, chloride and double salts of the latter can only be obtained in the form of oils.

Tetra-n-butylarsonium iodide, $(C_4H_9)_4AsI$, from arsenic and n-butyl iodide at 170-80°, forms small needles decomposing at 145-50°; soluble in water or alcohol and insoluble in ether.[379] The mercuriiodide consists of yellow needles, m. p. 109°; soluble in acetone, insoluble in water or

ether.[380] The *hydroxide* and *chloride* are obtained like the corresponding derivatives previously described. The mercurichloride is a radiating crystalline mass; the platinichloride, reddish-yellow crystals gradually darkening and finally decomposing at 220°; the aurichloride, needles melting indefinitely at 131°.[381]

Trimethylethylarsonium iodide, $(CH_3)_3(C_2H_5)AsI$, is prepared by heating ethylarsine with an excess of methyl iodide:

$$C_2H_5AsH_2 + 3CH_3I \longrightarrow (CH_3)_3(C_2H_5)AsI + 2HI.$$

It consists of lustrous needles softening at 300° and sintering at 320°; soluble in water, chloroform or hot alcohol, difficultly so in cold alcohol or concentrated potassium hydroxide solution and insoluble in ether.[382]

Trimethylallylarsonium iodide, $(CH_3)_3(C_3H_5)AsI$, is derived from methyl iodide and dimethylallylarsine.[331]

Trimethyl-ω-bromoethylarsonium bromide,

$$(CH_3)_3(CH_2Br.CH_2)AsBr,$$

from trimethylarsine and ethylene bromide in a closed vessel at 100-105°, crystallizes from hot alcohol in fine prismatic plates, m. p. 239°; very easily soluble in water but difficultly in cold alcohol. The corresponding picrate, m. p. 189°, is difficultly soluble in cold water or alcohol but more readily in hot. When heated with water in a closed vessel at 180° for four hours, the above bromoethyl compound is converted into *trimethyl-ω-hydroxyethylarsonium bromide,* a deliquescent solid melting at 219°, soluble in alcohol and insoluble in ether.[383] The corresponding *arsonium chloride,* $(CH_3)_3(CH_2OH.CH_2)AsCl$, is prepared from trimethylarsine by heating with glycol chlorhydrin at 120-5° for four hours in a closed vessel. It forms very deliquescent, prismatic crystals, m. p. 218-20°; very easily soluble in alcohol, slightly so in chloroform and insoluble in ether. Its aqueous solution yields no precipitate with hydrogen sulfide. It forms a crystalline mercurichloride; yields a white precipitate with Mayer's reagent; a brown, greasy precipitate with potassium iodide, and a voluminous white deposit with phosphotungstic acid. The corresponding *arsonium iodide* consists of deliquescent needles easily soluble in alcohol; the *sulfate* is also deliquescent, dissolves in alcohol, and melts at 240°; the *diiodosalicylate* is stable in air, easily soluble in water, insoluble in ether and melts at 140°; the *picrate,* prisms melting at 249°, is difficultly soluble in cold water or alcohol, readily in hot water or acetone and insoluble in ether or cold benzene. The *arsonium hydroxide,* $(CH_3)_3(CH_2OH.CH_2)As.OH$, prepared from the corresponding chloride in the usual manner, is a thick mass having the odor of trimethylarsine and reacting strongly alkaline. It is easily soluble in water or alcohol and insoluble in ether.[384]

Triethyl-ω-bromoethylarsonium bromide, $(C_2H_5)_3(CH_2Br.CH_2)AsBr$, is prepared by the interaction of triethylarsine and ethylene bromide in a sealed tube at 50° [21] or at 100-105°.[383] It forms rhombic dodecahedra readily soluble in water or hot alcohol and melting at 225°. With silver chloride it yields the corresponding *arsonium chloride;* heating with water at 180° converts it into the *hydroxyethylarsonium bromide,*[383] while moist silver oxide liberates hydrobromic acid, forming *triethylvinylarsonium hydroxide,* $(C_2H_5)_3(CH_2 = CH)As.OH$. This is in direct contrast with the corresponding phosphorus compound which under the same conditions yields triethyl-ω-hydroxyethylphosphonium hydroxide. When the above vinylarsonium hydroxide is neutralized with hydrochloric acid it yields the corresponding *chloride* which forms a platinichloride consisting of moderately soluble octahedra, and also a sparingly soluble, yellow, crystalline aurichloride.[21]

Triethyl-ω-hydroxyethylarsonium chloride,

$$(C_2H_5)_3(CH_2OH.CH_2)AsCl,$$

is prepared from triethylarsine and glycol chlorhydrin at 120-5°. It forms fine deliquescent needles very easily soluble in alcohol but insoluble in ether. The corresponding *diiodosalicylate* is stable in air, melts at 118°, is easily soluble in water or alcohol but insoluble in ether; the *triborate* is stable in air and easily soluble in hot water or alcohol; the *picrate* is fairly easily soluble in hot, difficultly so in cold water, insoluble in ether and melts at 152°. The corresponding *arsonium hydroxide,* prepared from the chloride in the usual manner, is a thick mass resembling the trimethyl homologue.[384]

Dimethyldiethylarsonium iodide, $(CH_3)_2(C_2H_5)_2AsI$, consists of colorless prisms obtained by the action of ethyl iodide on cacodyl in a sealed tube at ordinary temperature: [385]

$$(CH_3)_4As_2 + 2C_2H_5I \longrightarrow (CH_3)_2(C_2H_5)_2AsI + (CH_3)_2AsI.$$

It combines with iodine to the *triiodide*—brown needles with a metallic luster.[386] The corresponding *bromide* is derived from cacodyl and ethyl bromide at ordinary temperature; the *chloride* from cacodyl and ethyl chloride at 180°. The latter forms a platinichloride (orange-red needles), a mercurichloride (white needles) and an aurichloride (golden-yellow needles). The *hydroxide,* $(CH_3)_2(C_2H_5)_2As.OH$, is made from the bromide or iodide and moist silver oxide; [385] the neutral *sulfate* crystallizes in octahedra soluble in water or alcohol, while the *nitrate* forms deliquescent granules.

Dimethyldi-n-propylarsonium iodide, $(CH_3)_2(C_3H_7)_2AsI$, from cacodyl and n-propyl iodide at 140°, exists as pale yellow crystals. Its mercurichloride separates from hot water in white leaflets.[387]

Dimethyldiisopropylarsonium iodide, from dimethylarsine and isopropyl iodide; white crystals, m. p. 230°; soluble in chloroform.[388]

Dimethyldiallylarsonium iodide, $(CH_3)_2(C_3H_5)_2AsI$, from cacodyl and allyl iodide,[389] or from dimethylarsine and allyl iodide.[390]

Dimethyldiisobutylarsonium iodide, $(CH_3)_2(C_4H_9)_2AsI$, is made by heating dimethylarsine and isobutyl iodide in a sealed tube at 110° for five hours. It is a white crystalline solid, m. p. 155°; soluble in alcohol or chloroform, insoluble in ether.[391]

Dimethyldiisoamylarsonium iodide, $(CH_3)_2(C_5H_{11})_2AsI$, consists of leaflets obtained from cacodyl and isoamyl iodide.[392] With isoamyl bromide the corresponding *arsonium bromide* results.[393]

Dimethyldicetylarsonium iodide, $(CH_3)_2(C_{16}H_{33})_2AsI$, from dimethylarsine and cetyl iodide at 100° for five hours, is a white crystalline solid, m. p. 53-4°.[388]

Dimethyl-n-propylisoamylarsonium iodide, $(CH_3)_2(C_3H_7)(C_5H_{11})AsI$, from dimethyl-n-propylarsine and isoamyl iodide at 120°.[394]

Di-n-propyldiisoamylarsonium iodide, $(C_3H_7)_2(C_5H_{11})_2AsI$, is obtained from diisoamylarsine and n-propyl iodide at 160° for two hours.[394]

Methyltriethylarsonium iodide, $(CH_3)(C_2H_5)_3AsI$, forms white crystals on heating methyl arsine and ethyl iodide at 110° for eight hours.[355]

Methyltri(β-chlorovinyl)arsonium iodide, $(CH_3)(CHCl=CH)_3AsI$, exists as lustrous, colorless needles, m. p. 209°. It is formed by heating equimolar amounts of the tertiary arsine and methyl iodide in a sealed tube at 100° for 27 hours.[394]

Ethyl-tri-n-propylarsonium iodide, $(C_2H_5)(C_3H_7)_3AsI$, from ethylarsine and n-propyl iodide at 110° for three hours, melts at 237° with decomposition, and forms a yellow-white mercuriiodide.[154]

Ethyltriisopropylarsonium iodide, prepared like the n-isomer, decomposes upon heating according to the following reactions: [395]

$$(C_2H_5)(C_3H_7)_3AsI \longrightarrow (C_3H_7)_3As + C_2H_5I$$
$$2(C_2H_5)(C_3H_7)_3AsI \longrightarrow (C_3H_7)_3AsI_2 + C_4H_{10} + (C_3H_7)_3As$$

Ethyltriisoamylarsonium iodide, $(C_2H_5)(C_5H_{11})_3AsI$, from ethylarsine and isoamyliodide at 140° for eight hours, crystallizes from alcohol in compact crystals unmelted at 250°, easily soluble in isoamyl- or ethyl alcohol, difficultly in chloroform and insoluble in ligroin or acetone.[396]

2. *Ethylenehexaethyldiarsonium Compounds,*

$$(C_2H_5)_3\underset{\overset{|}{X}}{As}.CH_2 - H_2C.\underset{\overset{|}{X}}{As}(C_2H_5)_3.$$

Ethylenehexaethyldiarsonium bromide,

$$(C_2H_5)_3\underset{\overset{|}{Br}}{As}.CH_2 - H_2C.\underset{\overset{|}{Br}}{As}(C_2H_5)_3,$$

is prepared by the addition of triethylarsine and triethyl-ω-bromoethylarsonium bromide at 150°. With moist silver oxide it forms the corresponding *hydroxide,* a basic substance which forms salts with mineral acids. The *chloride* forms a double salt with platinic chloride, $[(C_2H_5)_3As.Cl.CH_2]_2PtCl_4$, a pale yellow precipitate difficultly soluble in water, and an aurichloride, $[(C_2H_5)_3As.Cl.CH_2]_2.2AuCl_3$—yellow crystals.[22]

By condensing triethyl-ω-bromoethylarsonium bromide with ammonia at 100°, *ethylenetriethylarsammonium bromide,*

$$(C_2H_5)_3\underset{\overset{|}{Br}}{As}.CH_2 - H_2C.\underset{\overset{|}{Br}}{N}H_3,$$

is obtained. This behaves like the previous compound. The platinichloride, $[(C_2H_5)_3(Cl)As.C_2H_4.NH_3.Cl]PtCl_4$, is obtained as needles from hot hydrochloric acid; the aurichloride,

$$[(C_2H_5)_3(Cl)As.C_2H_4.NH_3.Cl].2AuCl_3,$$

consists of yellow leaflets.[23]

Triethylarsine and triethyl-ω-bromoethylphosphoniumbromide combine at 100° to *ethylenehexaethylphospharsonium bromide,*

$$(C_2H_5)_3\underset{\overset{|}{Br}}{As}.CH_2 - H_2C.\underset{\overset{|}{Br}}{P}(C_2H_5)_3.$$

With silver oxide in the cold it forms the corresponding *hydroxide,* which decomposes upon warming according to the equation:

$$(C_2H_5)_3\underset{\overset{|}{OH}}{As}.CH_2 - H_2C.\underset{\overset{|}{OH}}{P}(C_2H_5)_3 \longrightarrow$$

$$(C_2H_5)_3\underset{\overset{|}{OH}}{P}.CH_2 - CH_2OH + (C_2H_5)_3As.$$

The base reacts with mineral acids, forming salts which crystallize in needles and readily form double salts; the platinichloride,

$$[(C_2H_5)_3As(Cl).C_2H_4.P(Cl)(C_2H_5)_3]PtCl_4,$$

crystallizes from hydrochloric acid in orange-red, triclinic prisms.[24]

E. Pentaalkyl Arsines, R_5As.

Pentamethylarsine, $(CH_3)_5As$, was obtained by Cahours in small amounts by the action of zinc dimethyl upon tetramethylarsonium iodide:

$$2(CH_3)_4AsI + Zn(CH_3)_2 \longrightarrow 2(CH_3)_5As + ZnI_2.$$

The main product of the reaction is trimethylarsine from which the less volatile pentaalkyl compound is separated by fractional distillation. The latter is very unstable, and is decomposed by both iodine and hydrochloric acid to the corresponding tetramethylarsonium compounds: [397]

$$(CH_3)_5As + I_2 \longrightarrow (CH_3)_4AsI + CH_3I$$
$$(CH_3)_5As + HCl \longrightarrow (CH_3)_4AsCl + CH_4.$$

Chapter III. Unsaturated Aliphatic Arsenicals.

It has been found that the hydrocarbons or acids of the acetylene series react with arsenic trihalides or a mixture of arsenious acid and thionyl chloride forming derivatives corresponding to the general formula, $\underset{\substack{|\\ X}}{RC} = \underset{\substack{|\\ AsX_2}}{CR'}$, which on subsequent treatment with water yield arsine-oxides, $\underset{\substack{|\\ X}}{RC} = \underset{\substack{|\\ AsO}}{CR'}$. With suitable oxidizing agents both these classes of compounds may be converted into the corresponding arsonic acids, $\underset{\substack{|\\ X}}{RC} = \underset{\substack{|\\ AsO(OH)_2}}{CR'}$.

Chloroarsinosoheptine, $C_7H_{12}Cl.AsO$, results upon refluxing heptine with arsenic trichloride (2 parts) at 100° for 16 hours. After distilling off the unchanged arsenic trichloride in vacuo, the oily residue is dissolved in moist ether, and treated with aniline until a filtered sample gives no further precipitate with aniline. The whole is finally filtered, and the ethereal solution washed first with water containing hydrochloric acid and then with pure water until the washings no longer react acid to congo. After drying over sodium sulfate, the ether is distilled off in vacuo, when the desired arsineoxide remains as a thick, dark liquid which slightly attacks the skin.[398]

Bromoarsinosooctine, $C_8H_{14}Br.AsO$, similarly prepared from octine and arsenic tribromide, is a dark brown, oily liquid miscible in all proportions with ether, chloroform or benzene.[398]

Phenylpropiolic acid and arsenic trichloride react as above to form colorless leaflets easily soluble in hot acetone, chloroform or benzene, less so in ether and insoluble in water. When arsenic tribromide is employed there are obtained yellowish-brown crystals, m. p. 255-8°; soluble in acetone or benzene, practically insoluble in petroleum ether and entirely so in water. With caustic alkalis at low temperature the above two propiolic acid derivatives yield the corresponding alkali salts.[399]

Chloroarsinostearolic acid, $C_{18}H_{32}O_2Cl.AsO$, is prepared by heating stearolic acid with arsenic trichloride in a closed vessel at 140° for six hours, and removing the unchanged inorganic arsenic from the reaction-

product either by distilling in vacuo or by dissolving the whole in ether, and shaking repeatedly with water. The ethereal solution is carefully concentrated, poured into cold aqueous caustic potash, and the resulting solution finally acidified with hydrochloric acid. The precipitated fatty mass is then dissolved in ether, the solution dried with calcium chloride and the solvent evaporated off.[400] The same product may be obtained by heating stearolic acid with powdered arsenic and sulfuryl chloride at 145° for 5-6 hours.[401] By purification with petroleum ether, it is obtained as a brownish, semi-fluid product insoluble in water but soluble in the usual organic solvents. The strontium salt, $(C_{18}H_{31}O_2Cl.AsO)_2Sr$, prepared by dissolving the acid in alcohol and pouring into a well-cooled methyl alcoholic solution of strontium chloride saturated with ammonia, is a flesh-colored powder insoluble in water. The calcium salt has essentially the same properties. The ethyl ester is derived from the acid by warming with ethyl alcohol and sulfuric acid. It is a brown oil easily soluble in chloroform or benzene but insoluble in water.[402]

Bromoarsinosostearolic acid is a semi-solid mass obtained by passing hydrogen bromide into a mixture of stearolic acid, arsenic trioxide and anhydrous magnesium sulfate for one hour at 135°, and maintaining the whole at the same temperature for ten more hours.[403]

Chloroarsinosobehenolic acid, $C_{22}H_{40}O_2Cl.AsO$, may either be prepared like the stearolic acid derivative;[404] by passing dry hydrogen chloride into a mixture of behenolic acid, arsenic trioxide and anhydrous cupric sulfate at 140°, until all of the arsenic trioxide has disappeared and then heating for 5-6 hours at the same temperature;[403] or by heating a mixture of behenolic acid and arsenic trioxide with thionyl chloride at 135° for six hours, and treating with alkali.[401] The product is a pale brownish-red oil insoluble in water, but easily soluble in alcohol, ether, benzene, chloroform or olive oil. When heated in a test tube, it decomposes with the formation of an arsenic mirror. On treating its alcoholic solution with normal potassium hydroxide and warming on a water-bath for two hours it decomposes, yielding behenolic acid, which may be isolated by cooling the liquid and saturating with hydrochloric acid. It reacts vigorously with thionyl chloride, the product condensing with aniline to form *chloroarsinosobehenolanilide*.[402] Its alkali salts resemble soaps and are soluble in water. A carefully neutralized solution of the potassium salt may be kept for several hours without decomposition, but in the presence of an excess of alkali, hydrolysis occurs. The strontium salt, known as "Elarson," is prepared like the corresponding salt of stearolic acid, and is insoluble in water, difficultly soluble in alcohol, ether or olive oil, decomposes when strongly heated, and yields the acid derivative when treated with cold dilute hydrochloric acid in the presence of a little ether. The calcium salt has also been prepared.[405] The

ferric salt is a red-brown powder insoluble in water or alcohol; the basic ferric salt is a light-brown powder insoluble in water or alcohol,[406] while the yohimbine salt is a faintly colored powder, m. p. 90°, soluble in water, alcohol or acetone.[285] The methyl ester, from methyl behenolate and either arsenic trichloride or arsenic trioxide and thionyl chloride,[402] or from chloroarsinosobehenolic acid by warming with methyl alcohol and concentrated sulfuric acid,[407] is a brown oily liquid easily soluble in ether or benzene but difficultly so in alcohol.[402]

Chloroarsinosobehenolic anhydride, from behenolic anhydride and arsenic trichloride, is a brown, fairly solid mass easily soluble in benzene or chloroform.[402]

Bromoarsinosobehenolic acid is a brown, semi-solid compound prepared like the chloro compound from arsenic tribromide.[408] Its anhydride is derived from the above acid by dissolving in benzene, treating successively with pyridine and a 25 per cent phosgene-benzene solution, and allowing to stand for two days. It is a brown mass easily soluble in benzene or chloroform.[402]

Chloroheptinearsonic acid, $C_7H_{12}Cl.AsO(OH)_2$, is formed upon oxidizing the corresponding arsineoxide with hydrogen peroxide in acetone solution. It crystallizes from hot water in clusters of white needles melting at 115°. Its monosodium salt consists of lustrous white leaflets easily soluble in water.[398]

Bromooctinearsonic acid, $C_8H_{14}Br.AsO(OH)_2$, is either prepared from the arsineoxide like the preceding acid or directly from octine and arsenic tribromide. The latter two substances are warmed together on a steam-bath for 15 hours, the unchanged arsenic tribromide distilled off in vacuo, and the residue oxidized with bromine in dry carbon bisulfide solution. The product crystallizes from hot water in long, colorless, lustrous needles melting at 129-30°.[398]

The *methyl ester of chlorobehenolarsonic acid,*

$$C_{22}H_{39}(CH_3)O_2Cl.AsO(OH)_2,$$

is prepared by oxidizing the methyl ester of the corresponding arsinoso compound with bromine in carbon bisulfide solution at low temperature, and purifying through the strontium salt. The acid is a thick, yellowish oil decomposed by strong heating, and easily soluble in alcohol, ether, chloroform, benzene or petroleum ether. On boiling with methyl alcoholic potash, the methyl group is split off, yielding a dibasic acid.[407]

An arsenical derivative of distearine has been obtained by heating it with alcoholic arsenic acid either under ordinary pressure or in vacuo for ten hours at 135-40°. The solidified reaction mass is dissolved in hot

carbon tetrachloride, filtered, the solvent distilled off, and the residue extracted with low-boiling petroleum ether to remove the unchanged distearine. It may also be prepared by grinding distearine together with arsenic acid and heating in an autoclave at 120-40° for 14 hours. The product is a fatty mass, m. p. 85-7°; easily soluble in chloroform, hot alcohol or ether but difficultly in petroleum ether.[409]

Chapter IV. Trivalent Aromatic Arsenicals.

A. Primary Derivatives.

1. *Aryl Arsines,* $RAsH_2$.—Although the corresponding aliphatic compounds possess very feebly basic properties, the unsubstituted primary aromatic arsines are entirely devoid of such characteristics. The products containing nuclear substituents, however, behave both like arsines and the corresponding non-arsenated organic compounds. They may be generally prepared by reducing arsonic acids, arsineoxides or arseno compounds with nascent hydrogen in acid solution:

$$RAsO(OH)_2 + 4H_2 \longrightarrow RAsH_2 + 3H_2O$$
$$RAsO + 2H_2 \longrightarrow RAsH_2 + H_2O$$
$$RAs = AsR + 2H_2 \longrightarrow 2RAsH_2.$$

In several instances it has been found possible to reduce arsonic acids electrolytically. The arsines are generally solids, with the exception of a few which are liquids. By regulated oxidation they may be converted into arseno compounds, arsineoxides or arsonic acids:

$$2C_6H_5AsH_2 + O_2 \longrightarrow C_6H_5As = AsC_6H_5 + 2H_2O$$
$$C_6H_5AsH_2 + O_2 \longrightarrow C_6H_5AsO + H_2O$$
$$2C_6H_5AsH_2 + 3O_2 \longrightarrow 2C_6H_5AsO(OH)_2.$$

When treated with halogens, replacement of the hydrogen occurs, yielding dihalogenated arsines:

$$RAsH_2 + X_2 \longrightarrow RAsHX.HX \longrightarrow RAsHX + HX \xrightarrow{X_2} RAsX_2.HX \longrightarrow RAsX_2 + HX;$$

while with alkyl halides they form aryltrialkylarsonium halides:

$$RAsH_2 + 3R'X \longrightarrow RR'_3AsX + 2HX.$$

The arsines form various arseno derivatives with compounds of the type $RAsO$, $RAsCl_2$, $RSbO$, $RSbCl_2$, $SbCl_3$ and $BiCl_3$ or $BiBr_3$:

$$RAsH_2 + RAsO \longrightarrow RAs = AsR + H_2O$$
$$RAsH_2 + RAsCl_2 \longrightarrow RAs = AsR + 2HCl$$
$$RAsH_2 + SbCl_3 \longrightarrow RAs = SbCl + 2HCl.$$

They may also be condensed with aldehydes, forming bis-α-hydroxytertiary arsines, tetrahydro-1,4,2,5-dioxdiarsines or arseno compounds, depending upon the conditions of the experiment.

carbon tetrachloride, filtered, the solvent distilled off, and the residue extracted with low-boiling petroleum ether to remove the unchanged distearine. It may also be prepared by grinding distearine together with arsenic acid and heating in an autoclave at 120-40° for 14 hours. The product is a fatty mass, m. p. 85-7°; easily soluble in chloroform, hot alcohol or ether but difficultly in petroleum ether.[409]

Phenylarsine, $C_6H_5AsH_2$.—Pure calcium phenylarsonate is mixed in a reflux apparatus with an excess of amalgamated zinc dust, the mixture covered with water and a layer of ether, and reduction effected by adding hydrochloric acid at the rate of 5-10 drops per minute. The ethereal layer is then dried over calcium chloride and distilled, the arsine coming over at 93°/70 mm. It is preserved in an atmosphere of carbon dioxide.[410, 411] The arsine may also be prepared from phenylarsonic acid by reducing either in a similar manner,[412] or electrolytically in an aqueous alcoholic hydrochloric acid medium.[413] The product is a colorless, highly refractive oil, b. p. 148°/760 mm., 93°/70 mm.; d^{25}_{25}, 1.356; has an odor like phenylisocyanide, but on dilution it resembles that of hyacinths; is readily soluble in alcohol, ether or carbon bisulfide, and oxidizes on exposure to air, forming arsenobenzene, phenylarsineoxide and phenylarsonic acid. It produces painful blisters on coming in contact with the skin, and is highly irritating to the mucous membrane. Heated for three hours at 240° in a sealed tube with carbon dioxide, it decomposes into triphenylarsine:

$$3C_6H_5AsH_2 \longrightarrow (C_6H_5)_3As + As_2 + 3H_2.$$[411]

With bromine it yields bromobenzene and arsenic tribromide, phenyldibromoarsine being formed as an intermediate product:

$$C_6H_5AsH_2 + 2Br_2 \longrightarrow C_6H_5AsBr_2 + 2HBr \xrightarrow{Br_2} C_6H_5Br + AsBr_3;$$

with iodine it forms phenyldiiodoarsine and phenylarsonic acid:

$$2C_6H_5AsH_2 + 10I + 3H_2O \longrightarrow C_6H_5AsI_2 + C_6H_5AsO_3H_2 + 8HI;$$

while with alkyl iodides phenyltrialkylarsonium iodides result.

Various aldehydes are reduced by the arsine with the formation of arsenobenzene and either the corresponding alcohol or other reduction products. Thus, with benzaldehyde, anisaldehyde, p-chlorobenzaldehyde or cinnamic aldehyde the reaction proceeds according to the following equation:

$$2C_6H_5AsH_2 + 2RCHO \longrightarrow C_6H_5As = AsC_6H_5 + 2RCH_2OH;$$

with m-nitrobenzaldehyde, the products are arsenobenzene and an unidentified substance containing a reduced nitro group, the latter assumption being based on the fact that phenylarsine reduces nitrobenzene, forming hydrazobenzene and arsenobenzene:

$$4C_6H_5NO_2 + 10C_6H_5AsH_2 \longrightarrow 2C_6H_5NH.HNC_6H_5 + 5C_6H_5As = AsC_6H_5 + 8H_2O;$$

with crotonic or salicyl aldehyde there are obtained arsenobenzene and other products as yet unidentified, while with chloral or chloral hydrate the end products are acetylaldehyde and phenyldichloroarsine:

$$3C_6H_5AsH_2 + 2CCl_3.CHO \longrightarrow 3C_6H_5AsCl_2 + 2CH_3CHO.$$

)uring the latter reaction a slight amount of arsenobenzene also results ue to the interaction of phenylarsine and the dichloroarsine.[415]

The arsine has been condensed with acetaldehyde, paraldehyde, proionaldehyde, butyraldehyde, isovaleraldehyde, n-heptylaldehyde, benaldehyde, p-chlorobenzaldehyde, p-methoxybenzaldehyde and o-carboxyiethoxybenzaldehyde to form the corresponding bis-(α-hydroxy alkyl or ryl) phenylarsines; and with paraformaldehyde, acetaldehyde, propionldehyde, butyraldehyde, isovaleraldehyde and furfural, yielding tetraydro-1,4,2,5-dioxdiarsines.[416, 417]

4-Methylphenylarsine, $(CH_3)C_6H_4AsH_2$, obtained by reducing -tolylarsonic acid according to the method employed for the preparaion of phenylarsine, is a colorless liquid, b. p. 113.5°/44 mm. By freezig it can be obtained as white lustrous plates, m. p. 20°.[418] It has been ondensed with both paraldehyde and benzaldehyde.

2-Methylphenylarsine, prepared like the preceding isomer, is a coloress oil, b. p. 121°/93 mm. On exposure to air it rapidly oxidizes to the rseno compound, which can be separated from traces of the arsonic cid formed at the same time by means of sodium hydroxide.[419] Conensation products of the arsine with paraldehyde and benzaldehyde have een prepared.

Benzylarsine, $C_6H_5.CH_2AsH_2$, is made from the corresponding arsonic cid like the previous compounds.[154] It is a faintly yellow liquid boiling t 140°/262 mm., and forming a black, amorphous platinichloride, $C_6H_5AsH_2.PtCl_4$. Heated with hydriodic acid at 140° for one hour, he arsine yields hydrogen, a brown-black solid and an oil (evidently enzyldiiodoarsine); with bromine at ordinary temperature, hydrogen, ransparent crystals and a heavy dark oil result. On exposure to air he arsine is oxidized to benzylarsonic acid and a red product, arsenohenylmethane ($C_6H_5.CH_2.As{=}As.H_2CC_6H_5$), while heating in a ealed tube for two hours at 250° produces a black polymer of arsenohenylmethane, $(C_7H_7As)_4$:

$$4C_6H_5CH_2AsH_2 \longrightarrow (C_6H_5CH_2As)_4 + 4H_2.$$

4-Chlorophenylarsine, $ClC_6H_4AsH_2$, from 4-chlorophenylarsonic acid y reduction with zinc amalgam and concentrated hydrochloric acid in nethyl alcohol,[420] is a liquid, b. p. 116°/33 mm., 159°/200 mm.; distillble in steam. When cooled it crystallizes in thin, transparent leaves, n. p. 30.5-30.7°.

2-Chlorophenylarsine, prepared like phenylarsine, boils at 206° and s distillable in steam.[421]

4-Aminophenylarsine, $(H_2N)C_6H_4AsH_2$.—p-Arsanilic acid dissolved n methyl alcohol is reduced with zinc dust and concentrated hydro-

chloric acid, the filtrate rendered alkaline, distilled in steam and the distillate extracted with ether. After distilling off the solvent, the arsine remains as a colorless oil, b. p. 132°/10 mm.; soluble in alcohol, ether or glacial acetic acid but only sparingly in water. It oxidizes very readily in the air, turning yellow and forming 4,4′-diaminoarsenobenzene. Upon heating it darkens and finally decomposes at about 130°.[422] The arsine may also be obtained by the electrolytic reduction of the above arsonic acid in mineral acid solutions with the exclusion of air.[423]

4-Acetylaminophenylarsine, $(CH_3CO.HN)C_6H_4AsH_2$, obtained by reducing the corresponding arsonic acid with zinc dust and hydrochloric acid, is a white powder soluble in methyl alcohol or dilute hydrochloric acid.[424]

N-(p-Arsylphenyl)glycine, [*Phenylglycine-4-arsine*],

$$(HOOCCH_2.HN)C_6H_4AsH_2.$$

The corresponding arsonic acid is dissolved in concentrated hydrochloric acid and reduced at moderate temperature by the gradual introduction of zinc dust. A yellow precipitate is first formed; this dissolves to a yellow solution which finally becomes colorless. Sodium acetate is then added to the filtrate, a white precipitate of the zinc salt of phenylglycine-4-arsine separating out. This is warmed with an excess of aqueous sodium carbonate solution, the resulting zinc carbonate filtered off, and the filtrate acidified with hydrochloric acid. The free arsine separates as a faint yellow precipitate very difficultly soluble in water, alcohol or ether. It assumes a deeper yellow coloration on exposure to air, and decomposes when heated at 100°.[422]

4-Hydroxyphenylarsine, $HO.C_6H_4AsH_2$, results upon reducing the corresponding arsonic acid in methyl alcohol. It is isolated by filtering the reaction mixture, extracting the filtrate with ether, removing the arsine from the extract by means of caustic soda, and reprecipitating by a current of carbon dioxide. It is a white powder gradually turning yellow and finally red due to oxidation to 4,4′-dihydroxyarsenobenzene. It is soluble in caustic soda, sparingly so in water, alcohol or ether; darkens at 75°, and decomposes at 155° without melting.[422]

3-Amino-4-hydroxyphenylarsine, $(H_2N)(HO)C_6H_3AsH_2$, — 3,3′-Diamino-4,4′-dihydroxyarsenobenzene dihydrochloride (arsphenamine) is suspended in concentrated hydrochloric acid and reduction effected by gradually adding zinc dust at 40°. After dilution with water, the excess zinc dust is filtered off, the filtrate first treated with saturated sodium acetate solution, and then extracted with ether. The ethereal layer is separated, filtered and the filtrate evaporated to dryness in an atmos-

phere of nitrogen, when a white crystalline deposit of the arsine is obtained. The crude product is purified by repeatedly dissolving in caustic soda solution and reprecipitating with glacial acetic acid at low temperature in an atmosphere of nitrogen. A variation of this procedure consists in adding an excess of methyl alcoholic hydrochloric acid to the above filtered ethereal extract, evaporating the resulting solution to dryness in an atmosphere of nitrogen, dissolving the residue in a slight amount of water, and precipitating the arsine with alkali. The whole is then extracted with ether and the ethereal solution evaporated to dryness as in the previous instance.[425]

The same arsine has also been obtained by reducing 3-nitro-4-hydroxyphenylarsonic acid with zinc and concentrated hydrochloric acid at moderate temperature. At the beginning of the reduction a precipitate forms which finally redissolves to a dark solution. This is diluted with water, the solution warmed until colorless and then filtered. On cooling, the double zinc salt separates; this is decomposed with sodium acetate and the arsine removed by extraction with ether. From the latter it is extracted by means of caustic soda solution and reprecipitated by acetic acid.[422] The yields thus obtained are very small.

A modification of this method consists in dissolving the nitro arsonic acid in ethyl alcohol, reducing with zinc dust and hydrochloric acid, and introducing the filtrate into aqueous sodium acetate solution. After standing for some time in the cold, the arsine separates out.[426]

The pure product is a white powder with a yellowish tint, soluble in dilute caustic soda, hydrochloric acid, ether, methyl or ethyl alcohol, and insoluble in acetone, benzene, toluene, chloroform, carbon tetrachloride or carbon bisulfide. On heating it decomposes without melting.[425] The arsine forms an N-condensation product with 3-sulfobenzaldehyde in alkaline solution,[427] and yields coördination products with auric chloride, silver nitrate or copper chloride. The gold compound is a brown powder readily soluble in water, alkalis, acids or methyl alcohol; the silver derivative is a black powder soluble in water, acids or alkalis, while the copper compound is a yellowish-red powder soluble in concentrated alkalis. They are prepared by bringing the two constituents together in methyl alcohol-hydrochloric acid and precipitating with ether.[428]

3-Carbethoxyamino-4-hydroxyphenylarsine,

$$(C_2H_5OOC.HN)(HO)C_6H_3AsH_2,$$

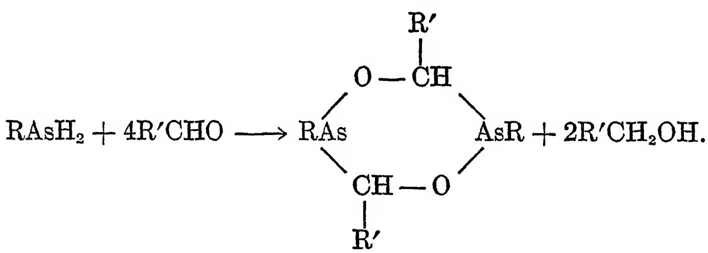
is a white crystalline powder, m. p. 155-60°; prepared by the electrolytic reduction of the corresponding arsonic acid. By treating with sulfurous acid and subsequently hydrolyzing, 3-amino-4-hydroxyphenylarsine is obtained.[429] With palladous chloride in methyl alcohol-glacial acetic acid solution it forms a black addition product which is precipitated by ether.[428]

4-Carboxyphenylarsine, $HOOC.C_6H_4AsH_2$, results when the corresponding arsonic acid is reduced with zinc dust and hydrochloric acid in methyl alcoholic solution. It crystallizes from ether in colorless, compact, prismatic crystals, m. p. 79-80°; readily soluble in alcohol, acetone, ether, glacial acetic acid, chloroform or hot water, less so in benzene or ligroin. It rapidly oxidizes in the presence of moisture to the arseno derivative, but when preserved for a prolonged period in a dry condition, it is converted into the arsineoxide.[106]

Methyl ester of 3-carboxy-4-aminophenylarsine (*Methylanthranilylarsine*), $(CH_3OOC)(H_2N)C_6H_3AsH_2$, prepared from the corresponding arsonic acid by reduction with zinc and hydrochloric acid, is a difficultly soluble, yellow powder.[430]

2. *Condensation Products of Aryl Arsines with Aldehydes.*[416, 417]—Under certain definite conditions it is possible to direct the course of reaction between primary aromatic arsines and aldehydes in three different ways, according to the following equations:

1. $RAsH_2 + 2R'CHO \longrightarrow RAs(CH.OH.R')_2.$

2. 

3. $2RAsH_2 + 2R'CHO \longrightarrow RAs{=}AsR + 2R'CH_2OH.$

The first reaction readily takes place when the arsine and an excess of aldehyde (aromatic or aliphatic) are vigorously stirred together at low temperature in the presence of a little concentrated hydrochloric acid, either with or without a solvent. Although anhydrous hydrochloric acid gas is most efficient in the case of aromatic aldehydes, it cannot be employed with aliphatic aldehydes. The resulting bis-α-hydroxytertiary arsines, $RAs(CHOHR')_2$, which are generally oils in the aliphatic series and solids in the aromatic, decompose on strong heating over a free flame into aldehyde and arsine, the latter becoming immediately oxidized to arsenobenzene in the presence of air. They are stable toward water, cold or hot dilute alkalis and cold dilute acids; are, as a rule, slowly oxidized in the air, more rapidly in carbon tetrachloride solution, and readily by oxidizing agents such as potassium permanganate or nitric acid, the products being an aryl arsonic acid and the respective aldehyde:

$$RAs(CHOHR')_2 + 3O \longrightarrow RAsO(OH)_2 + 2R'CHO.$$

The aliphatic derivatives may be titrated quantitatively with iodine in ether solution as follows:

$$RAs(CHOHR')_2 + 2I_2 \longrightarrow RAsI_2 + 2HI + 2R'CHO.$$

With the aromatic aldehyde derivatives iodine reacts slowly, but quantitative titration is impossible. Bromine reacts violently with these condensation products leaving a heavy reddish oil, which behaves like phenyldibromoarsine with nitric acid, yielding an arylarsonic acid and free bromine. The reaction is probably similar to that of iodine, although the formation of an aldehyde has not been proven. Chlorine also behaves like iodine, producing first an aryl dichloroarsine, which by the continued action of the halogen in the presence of water is oxidized to the arsonic acid. With phosphorus pentachloride aryl dichloroarsines and the parent aldehydes are formed:

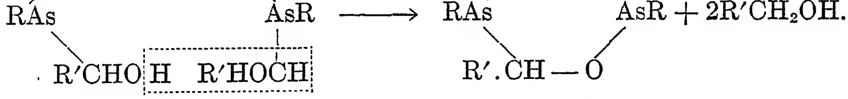
$$RAs(CHOHR')_2 + PCl_5 \longrightarrow RAsCl_2 + 2HCl + 2PCl_3 + 2R'CHO,$$

while phenyldichloroarsine produces arsenobenzenes and the original aldehydes:

$$C_6H_5As(CHOHR)_2 + C_6H_5AsCl_2 \longrightarrow C_6H_5As = AsC_6H_5 + 2HCl + 2RCHO.$$

In the cold without a solvent, in pyridine solution, or in the Schotten-Baumann reaction acid chlorides are without effect. Toward reducing and dehydrating agents (excepting anhydrous hydrogen chloride, acid chlorides, or anhydrides under certain conditions) these compounds are very stable. The aliphatic derivatives form unstable addition products with haloid acids and stable compounds with chloroplatinic acid, but do not react with the Grignard reagent.

The second type of compounds, tetrahydro-1,4,2,5-dioxdiarsines, can be obtained directly from primary aromatic arsines and aliphatic aldehydes by allowing a mixture of the components to remain for a day or two in the presence of anhydrous hydrogen chloride at ordinary temperature. Similar compounds with aromatic aldehydes have not yet been isolated. The reaction takes place in two steps: first, bis-α-hydroxytertiary arsines are formed, which subsequently condense to tetrahydro-1,4,2,5-dioxdiarsines by the loss of two molecules of alcohol, thus:



The same products may be obtained by the action of acetyl chloride, acetic anhydride or anhydrous hydrogen chloride upon bis-α-hydroxytertiary arsines prepared from aliphatic aldehydes.

The dioxdiarsines are stable toward water, dilute acids or alaklis and even hot 10 per cent alcoholic caustic potash. They are oxidized by air to aryl arsineoxides and aldehydes, while with stronger oxidizing agents such as nitric acid, aryl arsonic acids and aldehydes are obtained. With iodine in ether solution they decompose to aldehydes and aryl diiodoarsines, while with phosphorus pentachloride they yield aryl dichloroarsines. They are decomposed by haloid acids, and form double salts with chloroplatinic acid or cupric chloride.

The reduction of aldehydes by aromatic primary arsines as represented by equation 3 takes place either at higher temperature with or without a catalyst, or on standing for a long time at room temperature without a catalyst. If, however, the aldehydes and arsines are mixed in proportions different from those indicated in the equation, the reactions take place in a somewhat different way and more complex products are formed.

Bis-(α-hydroxyalkyl or aryl) arylarsines.

Bis-(α-hydroxyethyl)phenylarsine, $C_6H_5As(CHOHCH_3)_2$.—Prepared from phenylarsine, acetaldehyde or paraldehyde and a slight amount of concentrated hydrochloric acid. It is a colorless oil; d $\frac{25}{25}$, 1.252; n $\frac{25}{D}$, 1.5619. With hydriodic acid it forms a yellow hydriodide, m. p. 94-6°; insoluble in water, slightly soluble in organic solvents and stable toward alkali; the hydrobromide melts at 117-8°; the chloroplatinate, $C_6H_5As(CHOHCH_3)_2.H_2PtCl_6$, is a pale yellow powder, m. p. 169-70°.[431]

Bis-(α-hydroxy-n-propyl)phenylarsine, $C_6H_5As(CHOHC_2H_5)_2$, is a colorless oil; d $\frac{25}{25}$, 1.176; n $\frac{25}{D}$, 1.5425; its chloroplatinate melts at 148-9°.[432]

Bis-(α-hydroxy-n-butyl)phenylarsine, $C_6H_5As(CHOHC_3H_7)_2$, colorless oil, b. p. 187°/10 mm.; d $\frac{25}{25}$, 1.116; n $\frac{25}{D}$, 1.5271; hydriodide, m. p. 157-8°; hydrobromide, m. p. 111-12°; chloroplatinate, m. p. 119-21°.[432]

Bis-(α-hydroxyisovaleryl)phenylarsine, $C_6H_5As(CHOHC_4H_9)_2$, colorless oil, b. p. 170°/6 mm.; d $\frac{25}{25}$, 1.079; n $\frac{25}{D}$, 1.5202. By strong cooling and subsequent recrystallization from ether it is obtained as needles, m. p. 62°; chloroplatinate, m. p. 84-5°.[432]

Bis-(α-hydroxy-n-heptyl)phenylarsine, $C_6H_5As(CHOHC_6H_{13})_2$, b. p. 263-4°/2 mm.; d $\frac{25}{25}$, 1.069; n $\frac{25}{D}$, 1.4650. Upon freezing it solidifies but does not crystallize.[432]

Bis-(α-hydroxybenzyl)phenylarsine, $C_6H_5As(CHOHC_6H_5)_2$, white, silky needles, m. p. 193°; insoluble in water, slightly soluble in hot alcohol or ether, more readily in hot benzene or chlorobenzene.[433]

Bis-(α-hydroxy-4-chlorobenzyl)phenylarsine,

$$C_6H_5As(CHOHC_6H_4Cl)_2,$$

colorless needles from chlorobenzene, m. p. 164°; more soluble in the usual organic solvents than the previous compound.[433]

Bis-(α-hydroxy-4-methoxybenzyl)phenylarsine,

$$C_6H_5As(CHOHC_6H_4OCH_3)_2,$$

yellowish oil insoluble in water, readily soluble in organic solvents except petroleum ether.[433]

Bis-[o-(carboxymethoxy)-α-hydroxybenzyl] phenylarsine,

$$C_6H_5As(CHOHC_6H_4OCH_2COOH)_2,$$

colorless powder, m. p. 145-7° with loss of carbon dioxide; soluble in glacial acetic acid. It forms a disodium salt.[434]

Bis-(α-hydroxyethyl)p-tolylarsine, $CH_3.C_6H_4As(CHOHCH_3)_2$. — When a mixture of paraldehyde, p-tolylarsine and a few drops of hydrochloric acid are allowed to stand for 15 hours there is obtained a colorless oil, b. p. 176-7°/22 mm.; d. $\frac{18}{25}$, 1.2331; n $\frac{20}{D}$, 1.5570. It oxidizes readily on exposure to air.[435]

Bis-(α-hydroxybenzyl)p-tolylarsine, $CH_3.C_6H_4As(CHOHC_6H_5)_2$, white needles from benzene-alcohol mixture, melting at 208°.[418]

Bis-(α-hydroxyethyl)o-tolylarsine, a colorless oil, b. p. 165°/21 mm.; d $\frac{25}{25}$, 1.244; n $\frac{30}{D}$, 1.5573. It has a slightly greater tendency to oxidize than other analogous compounds.[419]

Bis-(α-hydroxybenzyl)o-tolylarsine, white needle-like crystals from ether, m. p. 140°.[419]

Bis-(α-hydroxyethyl)4-chlorophenylarsine, $ClC_6H_4As(CHOHCH_3)_2$, a colorless oil, b. p. 183°/23 mm.; d $\frac{25}{25}$, 1.336; n $\frac{25}{D}$, 1.5728.[436]

Bis-(α-hydroxybenzyl)4-chlorophenylarsine,

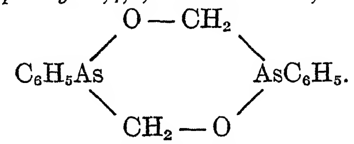
$$ClC_6H_4As(CHOHC_6H_5)_2,$$

from 4-chlorophenylarsine and benzaldehyde; white, silky needles from chlorobenzene-alcohol mixture, m. p. 218-218.5°.[436]

Bis-(α-hydroxybenzyl)2-chlorophenylarsine separates from alcohol or ether as white crystals melting at 146-7°.[421]

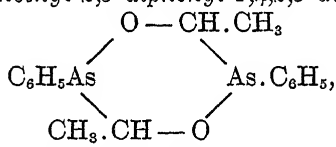
Tetrahydro-1, 4, 2, 5-dioxdiarsines.

Tetrahydro-2,5-diphenyl-1,4,2,5-dioxdiarsine,



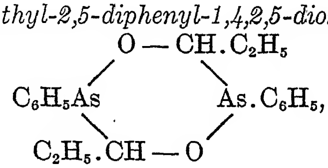
Obtained from paraformaldehyde, phenylarsine and concentrated hydrochloric acid as a colorless oil, b. p. 215-6°/9 mm.; $d\frac{25}{25}$, 1.547; $n\frac{25}{D}$, 1.6522; readily oxidizing in air.[434]

Tetrahydro-3,6-dimethyl-2,5-diphenyl-1,4,2,5-dioxdiarsine,



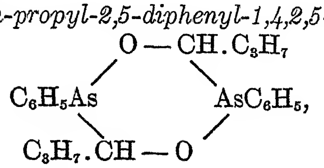
is a colorless oil, b. p. 257°/10 mm. with slight decomposition, $d\frac{25}{25}$, 1.369; $n\frac{25}{D}$, 1.6332. Prepared either from phenylarsine, acetaldehyde and hydrogen chloride; by heating bis-(α-hydroxyethyl)phenylarsine with half its weights of acetic anhydride under a reflux condenser in an oil bath at 140-50° for seven hours, or by merely allowing bis-(α-hydroxyethyl)phenylarsine to stand for a few days in the presence of anhydrous hydrogen chloride and then distilling. The chloroplatinate melts at 130-1°; the cuprichloride at 150-2°.[437]

Tetrahydro-3,6-diethyl-2,5-diphenyl-1,4,2,5-dioxdiarsine,



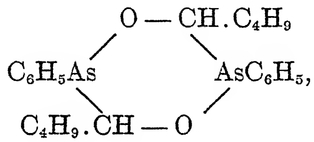
b. p. 212°/2 mm.; $d\frac{25}{25}$, 1.336; $n\frac{25}{D}$, 1.6217.[437]

Tetrahydro-3,6-di-n-propyl-2,5-diphenyl-1,4,2,5-dioxdiarsine,



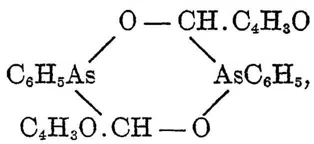
a pale yellow oil, b. p. 241-2°/2 mm.; d_{25}^{25}, 1.297; n_{D}^{25}, 1.5856; obtained from phenylarsine and n-butyraldehyde in the presence of gaseous hydrochloric acid, or by refluxing a mixture of acetic anhydride and bis-(α-hydroxy-n-butyl)phenylarsine for six hours.[437]

Tetrahydro-3,6-diisobutyl-2,5-diphenyl-1,4,2,5-dioxdiarsine,



from phenylarsine and isovaleraldehyde; an almost colorless oil comparatively stable in air; d_{25}^{25}, 1.296; n_{D}^{25}, 1.5869; chloroplatinate, m. p. 76-7°; cuprichloride, m. p. 78-9°.[438]

Tetrahydro-3,6-difuryl-2,5-diphenyl-1,4,2,5-dioxdiarsine,



from furfural and phenylarsine, is an insoluble powder resembling zinc dust in appearance, and burns without melting, leaving no residue.[438]

3. *Aryl Dihalogenated Arsines,* $RAsX_2$.—These compounds were first directly prepared by Michaelis from mercury diaryls and arsenic trichloride according to the equation:

$$HgR_2 + 2AsCl_3 \longrightarrow 2RAsCl_2 + HgCl_2.$$

This method, however, is limited to the preparation of dihalogenated arsines with hydrocarbon or phenol-ether residues. In addition, the preparation of mercury diaryls is associated with difficulties. On account of these disadvantages it was abandoned in favor of a more convenient method, which consists in heating tertiary aromatic arsines (easily prepared by condensing halogenated hydrocarbons and arsenic trichloride by means of metallic sodium) with arsenic trichloride:

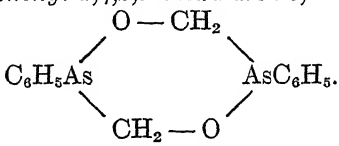
$$R_3As + AsCl_3 \longrightarrow 3RAsCl_2.$$

Later, Roeder and Blasi modified the mercury diaryl synthesis by employing arylmercurichlorides. These are very conveniently prepared by first forming arylmercuriacetates from benzene, its homologues, or various derivatives of the same, with mercuric acetate in acetic acid

Bis-(α-hydroxybenzyl)2-chlorophenylarsine separates from alcohol or ether as white crystals melting at 146-7°.[421]

Tetrahydro-1, 4, 2, 5-dioxdiarsines.

Tetrahydro-2,5-diphenyl-1,4,2,5-dioxdiarsine,



Obtained from paraformaldehyde, phenylarsine and concentrated hydrochloric acid as a colorless oil, b. p. 215-6°/9 mm.; d $\frac{25}{25}$, 1.547; n $\frac{25}{D}$, 1.6522; readily oxidizing in air.[434]

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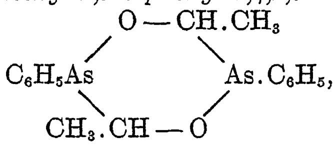

is a colorless oil, b. p. 257°/10 mm. with slight decomposition, d $\frac{25}{25}$, 1.369; n $\frac{25}{D}$, 1.6332. Prepared either from phenylarsine, acetaldehyde and hydrogen chloride; by heating bis-(α-hydroxyethyl)phenylarsine with half its weights of acetic anhydride under a reflux condenser in an oil bath at 140-50° for seven hours, or by merely allowing bis-(α-hydroxyethyl)phenylarsine to stand for a few days in the presence of anhydrous hydrogen chloride and then distilling. The chloroplatinate melts at 130-1°; the cuprichloride at 150-2°.[437]

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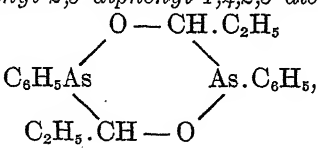
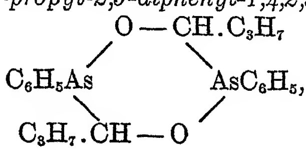


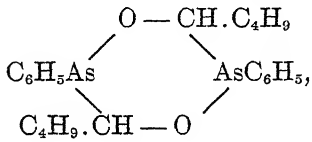
b. p. 212°/2 mm.; d $\frac{25}{25}$, 1.336; n $\frac{25}{D}$, 1.6217.[437]

Tetrahydro-3,6-di-n-propyl-2,5-diphenyl-1,4,2,5-dioxdiarsine,



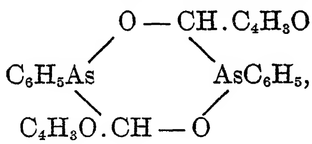
a pale yellow oil, b. p. 241-2°/2 mm.; $d\frac{25}{25}$, 1.297; $n\frac{25}{D}$, 1.5856; obtained from phenylarsine and n-butyraldehyde in the presence of gaseous hydrochloric acid, or by refluxing a mixture of acetic anhydride and bis-(α-hydroxy-n-butyl)phenylarsine for six hours.[437]

Tetrahydro-3,6-diisobutyl-2,5-diphenyl-1,4,2,5-dioxdiarsine,



from phenylarsine and isovaleraldehyde; an almost colorless oil comparatively stable in air; $d\frac{25}{25}$, 1.296; $n\frac{25}{D}$, 1.5869; chloroplatinate, m. p. 76-7°; cuprichloride, m. p. 78-9°.[438]

Tetrahydro-3,6-difuryl-2,5-diphenyl-1,4,2,5-dioxdiarsine,



from furfural and phenylarsine, is an insoluble powder resembling zinc dust in appearance, and burns without melting, leaving no residue.[438]

3. *Aryl Dihalogenated Arsines,* $RAsX_2$.—These compounds were first directly prepared by Michaelis from mercury diaryls and arsenic trichloride according to the equation:

$$HgR_2 + 2AsCl_3 \longrightarrow 2RAsCl_2 + HgCl_2.$$

This method, however, is limited to the preparation of dihalogenated arsines with hydrocarbon or phenol-ether residues. In addition, the preparation of mercury diaryls is associated with difficulties. On account of these disadvantages it was abandoned in favor of a more convenient method, which consists in heating tertiary aromatic arsines (easily prepared by condensing halogenated hydrocarbons and arsenic trichloride by means of metallic sodium) with arsenic trichloride:

$$R_3As + AsCl_3 \longrightarrow 3RAsCl_2.$$

Later, Roeder and Blasi modified the mercury diaryl synthesis by employing arylmercurichlorides. These are very conveniently prepared by first forming arylmercuriacetates from benzene, its homologues, or various derivatives of the same, with mercuric acetate in acetic acid

solution, and converting these into the corresponding chlorides by means of calcium chloride or some other suitable metallic chloride. The arylmercurichlorides react with arsenic trichloride at 100° according to the equation:

$$RHgCl + AsCl_3 \longrightarrow RAsCl_2 + HgCl_2.$$

In employing this method it is necessary to observe that any carboxyl, hydroxyl, amino or other groups present be first protected by alkylation or acylation, as otherwise the haloid acid formed will cause mercury to split off from the arylmercurichloride. The above reaction is practically a general one for the preparation of para substituted arsenicals, for it has been established that in mercurating aromatic compounds the metal enters the para or ortho position or both, but the para compound is much more readily reactive. It is probable, though it has not yet been definitely borne out by results, that ortho mercurated compounds may be converted into the corresponding dichloroarsines by reacting with arsenic trichloride in closed vessels under pressure.

In addition to these three direct methods, the following indirect procedures may also be employed for the preparation of primary aryl dihalogenated arsines:

1. The action of haloid acids upon aryl arsineoxides:

$$RAsO + 2HX \longrightarrow RAsX_2 + H_2O.$$

It is not necessary to isolate the arsineoxide itself, as a solution of the corresponding arsonic acid in the haloid acid yields the dihalogenated arsine upon reduction with sulfur dioxide. This procedure is particularly useful in obtaining dichloro derivatives.

2. The reduction of arsonic acids with hydriodic acid:

$$RAsO(OH)_2 + 4HI \longrightarrow RAsI_2 + 3H_2O + I_2.$$

3. The interaction of phosphorus trichloride and arsonic acids:

$$RAsO(OH)_2 + PCl_3 \longrightarrow RAsCl_2 + HPO_3 + HCl.$$

4. From arseno compounds by the action of halogens:

$$RAs = AsR + 2X_2 \longrightarrow 2RAsX_2.$$

The lower members of the series are colorless liquids which can be obtained in pure form by distillation under ordinary, but preferably under diminished pressure. The higher homologues are crystalline solids readily recrystallizable from various organic solvents. The unsubstituted members are very poisonous and have a powerfully irritating action upon the skin. They possess odors which are faint at ordinary temperatures but very penetrating and irritating at higher temperatures. The compounds are sparingly soluble in water, the higher members being

slowly converted into the arsineoxides while the lower homologues, as a rule, remain unaffected. Alkali hydroxides or carbonates easily dissolve the dihalogenated arsines, forming the corresponding arsineoxides. The dichloro compounds readily absorb chlorine yielding the corresponding arsinetetrachlorides, but no addition products are obtained with bromine, an excess of the latter causing a splitting off of arsenic, e. g.,

$$C_6H_5AsCl_2 + 2Br_2 \longrightarrow C_6H_4Br_2 + AsBrCl_2 + HBr.$$

Although they may be converted into arsonic acids by oxidizing agents, they are more resistant to such agents than the other trivalent aromatic organic arsenicals. An exception is furnished by benzyldichloroarsine which is unstable toward water, chlorine or atmospheric oxygen. The dihalogenated arsines are converted into arseno compounds either by reduction, e. g., with phosphorous acid, or by interaction with primary aromatic arsines:

$$2RAsX_2 + 2H_2 \longrightarrow RAs = AsR + 4HX$$
$$RAsX_2 + R'AsH_2 \longrightarrow RAs = AsR' + 2HX.$$

Sodium alcoholates or phenolates react with dichloroarsines, forming esters of arylarsenious acids:

$$RAsCl_2 + 2NaOR' \longrightarrow RAs(OR')_2 + 2NaCl.$$

Phenyldichloroarsine, $C_6H_5AsCl_2$, was first obtained by passing vapors of benzene and arsenic trichloride through a heated tube. The product thus obtained, however, is always admixed with diphenyl, which cannot be readily removed by distillation or crystallization.[439] It is more conveniently prepared by gradually adding mercury diphenyl with continuous stirring to an excess of arsenic trichloride, rapidly heating up to 254° and fractionating the filtrate.[439, 440] At lower temperatures the product is contaminated with phenylmercurichloride. Phenyldichloroarsine is also formed on heating phenylmercurichloride with arsenic trichloride at 100° for four or five hours;[441] by heating triphenylarsine with arsenic trichloride in a sealed tube at 250° for 30 hours, fractionating and collecting the portion coming over at 250-2°;[442] or by the action of chlorine upon arsenobenzene.[443] The product is a colorless, highly refractive, somewhat viscid liquid, b. p. 252-5°. At ordinary temperature it has a faintly unpleasant odor which at higher temperatures becomes very pungent. It has an extremely irritating action upon the skin; is unaffected by hot or cold water, but readily dissolves in aqueous caustic alkalis, yielding unstable dialkali salts of phenylarsenious acid, which are readily soluble in absolute alcohol, and are readily converted into the parent compound by means of concentrated hydrochloric acid. The dichloroarsine forms no addition product with oxygen either at ordinary or elevated temperatures; combines additively with chlorine forming phenylarsinetetrachloride, but does not unite with bromine, an excess of

the latter causing decomposition with the formation of dibromobenzene, arsenic bromodichloride and hydrobromic acid. Primary and secondary aliphatic amines react vigorously with the dichloroarsine, yielding compounds of the types $C_6H_5As\left\langle\begin{matrix}NH.R\\Cl\end{matrix}\right.$ and $C_6H_5As\left\langle\begin{matrix}NR_2\\Cl\end{matrix}\right.$ with liberation of hydrochloric acid. With butyl and dibutyl amines, for example, the compounds $C_6H_5As\left\langle\begin{matrix}NH.C_4H_9\\Cl\end{matrix}\right.$ and $C_6H_5As\left\langle\begin{matrix}N(C_4H_9)_2\\Cl\end{matrix}\right.$ respectively are obtained, while aniline yields a similar product, $C_6H_5As\left\langle\begin{matrix}NH.C_6H_5\\Cl\end{matrix}\right.$, which is readily hydrolyzed by moisture to phenylarsineoxide and aniline hydrochloride. Tertiary aliphatic amines form addition products, e. g., with triethylamine, the product $C_6H_5As\left\langle\begin{matrix}Cl\\Cl\\N(C_2H_5)_3\end{matrix}\right.$ results. With dimethylarsine there is also obtained a white crystalline addition product, $C_6H_5AsCl_2.(CH_3)_2AsH$, which is decomposed by atmospheric moisture.[444]

As-Phenylarsylenimine [*Phenylarsenimide*], $C_6H_5As=NH$.—When pure dry ammonia is passed into a benzene solution of phenyldichloroarsine, a vigorous reaction occurs, ammonium chloride separating:

$$C_6H_5AsCl_2 + 3NH_3 \longrightarrow C_6H_5As=NH + 2NH_4Cl.$$

After standing for some time, the clear solution is poured off and the residue extracted several times with benzene. The combined extracts are distilled on a water-bath under reduced pressure to remove the solvent, leaving a thick, yellow oil which partially crystallizes upon standing for several days. By the addition of absolute ether, the arsenimide is obtained as a beautiful white crystalline mass sintering at 265°, m. p. 270°; readily soluble in benzene or xylene and sparingly in ether or absolute alcohol, separating from the latter in leaflets. Water or dilute acids readily hydrolyze it to phenylarsineoxide and ammonia:

$$C_6H_5As=NH + H_2O \longrightarrow C_6H_5AsO + NH_3.$$ [445]

Phenyldibromoarsine, from phenylarsineoxide by warming with concentrated hydrobromic acid,[446, 447] is a colorless or faintly yellow liquid, b. p. 285° with slight decomposition; d. 2.0983/15°. It is unaffected

by water but is vigorously decomposed by bromine into bromobenzene and arsenic tribromide:

$$C_6H_5AsBr_2 + Br_2 \longrightarrow C_6H_5Br + AsBr_3.$$

Phenyldiiodoarsine is obtained from phenylarsineoxide [443] and concentrated hydriodic acid (d. 1.7). More recently it has been prepared from phenyldichloroarsine and sodium iodide in either absolute alcohol or acetone at ordinary temperature.[209, 171] According to Michaelis it is a red, oily liquid, while both Burrows and Steinkopf obtained it in the form of lemon-yellow needles, m. p. 15°; b. p. 190°/12 mm., 185°/10 mm. Phosphorous acid reduces it to diiodoarsenobenzene, $C_6H_5AsI — AsIC_6H_5$.

2-Methylphenyldichloroarsine, $(CH_3)C_6H_4AsCl_2$, from mercury di-o-tolyl and arsenic trichloride,[448, 449] is a colorless liquid, b. p. 264° in a current of carbon dioxide; has a faint aromatic odor at ordinary temperature which becomes very irritating at higher temperature. It is insoluble in water, soluble in alcohol, ether or benzene, and absorbs chlorine, forming 2-methylphenylarsinetetrachloride. The dichloroarsine does not combine additively with bromine, but when warmed with an excess of the latter is decomposed into dibromo-2-methylbenzene, arsenic-, hydrochloric and hydrobromic acids.

3-Methylphenyldichloroarsine results upon heating tri(3-methylphenyl) arsine with 10 parts of arsenic trichloride in a sealed tube at 300°. It is a colorless, highly refractive liquid, b. p. 270°, and readily absorbs chlorine, yielding the corresponding arsinetetrachloride.[450]

4-Methylphenyldichloroarsine.—Prepared from mercury di-p-tolyl and arsenic trichloride like its ortho isomer.[449, 451] More quantitative yields, however, are obtained by heating tri(4-methylphenyl) arsine with 10 parts of arsenic trichloride for 60 hours at 230-40°.[452] It exists as colorless, highly refractive plates, m. p. 31°; b. p. 267° in a current of carbon dioxide; has a faint, not unpleasant aromatic odor at ordinary temperatures, but when heated becomes very irritating; insoluble in water, readily soluble in alcohol, ether or benzene. With chlorine it forms 4-methylphenylarsinetetrachloride, but bromine decomposes it as in the case of the ortho isomer. It forms tertiary arsines with various zinc dialkyls, e. g., with zinc dimethyl there is produced p-tolyldimethylarsine.[453]

Benzyldichloroarsine, $C_6H_5.CH_2AsCl_2$.—From tribenzylarsine and arsenic trichloride by heating in a sealed tube at 160-80° for 12 hours.[454] It is a colorless oily liquid, b. p. 175°/50 mm.; cannot be solidified by freezing, and produces painful blisters upon the skin. It is far less stable

than purely aliphatic or aromatic dichloroarsines as evidenced by the following properties: water decomposes it into arsenic trioxide and either benzaldehyde or benzoic acid; chlorine converts it into benzyl chloride and arsenic trichloride, while atmospheric oxygen produces benzyl chloride and arsenic oxychloride:

$$C_6H_5.CH_2AsCl_2 + O \longrightarrow C_6H_5.CH_2Cl + AsOCl.$$

2,4-Dimethylphenyldichloroarsine (m-Xylyldichloroarsine),

$$(CH_3)_2C_6H_3AsCl_2,$$

is obtained from mercury di-m-xylyl and arsenic trichloride, or by heating tri-m-xylylarsine with arsenic trichloride in a sealed tube at 240°.[455] It exists as colorless needles, m. p. 42-3°; b. p. 215°/320 mm., 278° at ordinary pressure. On standing in the air it is gradually transformed into the arsineoxide, more readily upon warming in water. It is less stable toward water than the lower homologues. With chlorine it forms the corresponding arsinetetrachloride, while bromine decomposes it into dibromo-m-xylene, arsenic trichloride and hydrobromic acid.

2,5-Dimethylphenyldichloroarsine (p-Xylyldichloroarsine). — Prepared like the previous compound. Recrystallized from petroleum ether, it separates in tufts of needles, m. p. 63°; b. p. 285°.[456]

2,5-Dimethylphenyldiiodoarsine is obtained by dissolving the corresponding arsineoxide in warm hydriodic acid. It forms yellow crystals, m. p. 45°.[457]

The corresponding *dibromoarsine* cannot be obtained pure.

2,4,5 - Trimethylphenyldichloroarsine (Pseudocumyldichloroarsine), $(CH_3)_3C_6H_2AsCl_2$.—Tripseudocumylarsine is heated with four parts of arsenic trichloride at 200° for 48 hours and the product fractionated under 30 mm. pressure. It forms needles from ether, m. p. 82.5°; b. p. 190°/30 mm.[458]

4-Isopropylphenyldichloroarsine (p-Cumyldichloroarsine),

$$(C_3H_7)C_6H_4AsCl_2,$$

from tri-p-cumylarsine and arsenic trichloride at 170° for 48 hours,[459] is an oil, b. p. 170°/30 mm.

Tertiary-butylphenyldichloroarsine, $[(CH_3)_3C]C_6H_4AsCl_2$, is prepared by heating tri(tertiary-butylphenyl) arsine with arsenic trichloride for 24 hours at 200°. It is a colorless liquid, b. p. 175-80°/20 mm.[460]

α-Naphthyldichloroarsine, $C_{10}H_7AsCl_2$, may be obtained either by heating tri-α-naphthylarsine with arsenic trichloride at 270° for 40

hours,[461] or from mercury di-α-naphthyl and arsenic trichloride by heating in a reflux apparatus.[462] It crystallizes from petroleum ether as a white, crystalline powder, m. p. 63° (Michaelis), 68° (Steinkopf); b. p. 180°/5 mm.; soluble in alcohol or petroleum ether.

β-Naphthyldichloroarsine.—Since tri-β-naphthylarsine is obtained with difficulty, the most convenient method of preparation consists in boiling mercury di-β-naphthyl with arsenic trichloride in a reflux apparatus for one hour.[461] It forms warty aggregates of needles, m. p. 69°; soluble in ether, alcohol or benzene, and is slowly hydrolyzed by water to the arsineoxide and hydrochloric acid. By reduction with phosphorous acid, it is converted into arseno-β-naphthalene.

4-Phenylphenyldichloroarsine (Diphenyl-4-dichloroarsine),

$$(C_6H_5)C_6H_4AsCl,$$

m. p. 74°, is made by boiling the corresponding arsineoxide with concentrated hydrochloric acid.[463]

2-Bromophenyldichloroarsine, $BrC_6H_4AsCl_2$. — The corresponding bromoarsonic acid is reduced by means of sulfur dioxide in fuming hydrochloric acid solution with a slight amount of hydriodic acid as a catalyst. It is a reddish oil crystallizing from petroleum ether in colorless plates, m. p. 63°; b. p. 158°/12 mm.; readily soluble in organic solvents.[464]

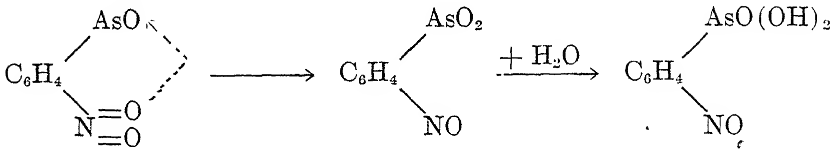
4-Iodophenyldiiodoarsine, $IC_6H_4AsI_2$.—Prepared by the action of concentrated hydriodic acid upon 4-iodophenylarsonic acid:

$$IC_6H_4AsO(OH)_2 + 4HI \longrightarrow IC_6H_4AsI_2 + 3H_2O + I_2.$$

It also results as a by-product in the preparation of 4-iodophenylarsonic acid from p-arsanilic acid.[465] It consists of golden-yellow needles, m. p. 80°; soluble in glacial acetic acid or the usual organic solvents, and yielding the corresponding arsineoxide with water, alkali hydroxides or carbonates.

2-Nitrophenyldichloroarsine, $(O_2N)C_6H_4AsCl_2$.—2-Nitrophenylarsineoxide is suspended in commercial ether, and alcoholic hydrochloric acid added drop by drop until a faintly yellow solution is obtained. From this, upon exposure to strong sunlight for several weeks in a sealed tube, a yellowish-brown crystalline deposit separates. The latter possesses the following characteristic properties: (1) it is readily soluble in sodium carbonate or bicarbonate, thereby resembling an arsonic acid; (2) analytical results correspond to the formula $C_6H_6O_4NAs$; (3) it is insoluble in boiling water, which is a distinction from 2-nitrophenylarsonic acid. Karrer regards it as a highly polymerized form of a nitroso compound

produced in the presence of water by the migration of an oxygen atom from the nitro group to the arsenious radical: [466]



3-Nitrophenyldichloroarsine.—Upon passing chlorine into a chloroform suspension of 3,3′-dinitroarsenobenzene, a solution results, from which upon evaporation, long needles of 3-nitrophenylarsinetetrachloride separate. By treating a chloroform solution of the latter with an excess of 3,3′-dinitroarsenobenzene, filtering and distilling off the solvent from the filtrate, the dichloroarsine remains as an oil, which when desiccated separates as small white crystals, m. p. 46-7°; unaffected by water.[467]

3-Nitrophenyldibromoarsine is prepared by adding bromine to a suspension of 3,3′-dinitroarsenobenzene in petroleum ether (b. p. 50° or below). It forms white crystals readily soluble in chloroform, sparingly so in petroleum ether, and unaffected by water.[467]

The corresponding *diiodoarsine* has not been obtained crystalline.[467]

3-Nitro-4-methylphenyldibromoarsine, $(O_2N)C_6H_3(CH_3)AsBr_2$, is prepared like the previous compound in a chloroform medium. It crystallizes in lustrous, brownish-white scales sintering at 260° with decomposition, readily soluble in alcohol, ether, chloroform or aqueous alkaline solutions, and forms no addition product with bromine.[468]

2,4-Dinitrophenyldichloroarsine, $(O_2N)_2C_6H_3AsCl_2$, is prepared from the corresponding arsineoxide and hydrochloric acid in alcoholic or ethereal medium.[469]

3-Nitro-4-aminophenyldiiodoarsine, $(H_2N)(O_2N)C_6H_3AsI_2$, from the corresponding arsonic acid by gently warming with concentrated hydriodic acid, melts at 96°.[85]

4-Aminophenyldichloroarsine hydrochloride, $(HCl.H_2N)C_6H_4AsCl_2$.—From the corresponding arsineoxide and hydrochloric acid;[470] or directly from sodium-4-aminophenylarsonate (atoxyl) by acidifying its concentrated aqueous solution with hydrochloric acid, filtering off the sodium chloride which separates, and saturating the filtrate with sulfur dioxide in the presence of a trace of hydriodic acid. After 12 hours the above hydrochloride begins to crystallize.[471] It is also obtained in impure form by the action of phosphorus trichloride upon 4-aminophenylarsonic acid.[472] The salt crystallizes in needles, m. p. 139-40°, decomposing at higher temperatures into arsenic trichloride and aniline:

$$(HCl.H_2N)C_6H_4AsCl_2 \longrightarrow AsCl_3 + C_6H_5NH_2.$$

It is readily soluble in water, methyl or ethyl alcohol, sparingly in acetone or ethyl acetate and insoluble in cold glacial acetic acid, ether, benzene or chloroform. The aqueous solution upon neutralization with ammonia yields the arsineoxide.

4-Aminophenyldibromoarsine hydrobromide results from the action of hydrobromic acid upon the arsineoxide. It is a yellow, crystalline mass, m. p. 134°; decomposing like the preceding compound at higher temperatures. It is readily soluble in water, acetone, methyl or ethyl alcohol, and sparingly so in cold glacial acetic acid, ether, ethyl acetate, chloroform or benzene.[473]

4-Aminophenyldiiodoarsine hydriodide can be prepared like the two preceding halogen compounds, but the best method consists in reducing 4-aminophenylarsonic acid with hydriodic acid. It is a yellow, crystalline powder, readily soluble in acetone, methyl or ethyl alcohol, very sparingly so in cold glacial acetic acid, ether, ethyl acetate, benzene or chloroform, and is hydrolyzed by water. When strongly heated it decomposes like the two previous compounds.[474]

4-Acetylaminophenyldichloroarsine semi-hydrochloride,

$$[(CH_3CO.HN)C_6H_4AsCl_2]_2.HCl,$$

is derived from 4-acetylaminophenylarsonic acid by suspending in dry ethyl acetate and reducing with phosphorus trichloride.[475] It crystallizes in wart-like aggregates, m. p. 137° with much foaming; soluble in acetone, glacial acetic acid, methyl or ethyl alcohol, sparingly in cold ethyl acetate and practically insoluble in water or ether. With aqueous caustic soda it forms the corresponding arsineoxide.

Phenylglycine-4-dichloroarsine hydrochloride (4-Dichloroarsinophenylglycine hydrochloride), $(HCl.HOOCCH_2NH)C_6H_4AsCl_2$.—A concentrated hydrochloric acid solution of phenylglycine-4-arsonic acid, to which a slight amount of hydriodic acid has been added, is saturated at — 10° with sulfur dioxide, the dichloroarsine hydrochloride separating as white crystals which decompose at 120°, are readily soluble in water or methyl alcohol and are converted into the arsineoxide by aqueous alkalis.[476] It is decomposed into 4-chloromercuriphenylglycine and arsenious acid by means of aqueous mercuric chloride.[477]

4-Dimethylaminophenyldichloroarsine hydrochloride,

$$[HCl(CH_3)_2N]C_6H_4AsCl_2,$$

from the corresponding arsineoxide and hydrochloric acid, crystallizes in white needles, m. p. 116°; readily soluble in water or dilute hydrochloric acid but sparingly in the concentrated acid. The corresponding *dibromo-*

arsine hydrobromide is similarly prepared. It is soluble in alcohol, from which it is reprecipitated by ether.[478] The *diiodoarsine hydriodide* may be obtained either from the arsineoxide and hydriodic acid, or by adding potassium iodide to the corresponding dichloroarsine hydrochloride in aqueous or alcoholic solution. It is a yellow, unstable precipitate, turning deep red upon drying.[479]

2-Chloro-4-dimethylaminophenyldichloroarsine hydrochloride,

$$[HCl(CH_3)_2N]C_6H_3Cl.AsCl_2,$$

prepared from the corresponding arsineoxide and concentrated hydrochloric acid, is easily soluble in alcohol, acetone or water; melts at 116°, and is converted into the arsineoxide by aqueous alkalis.[480]

2-Bromo-4-dimethylaminophenyldichloroarsine hydrochloride melts at 115°; the corresponding *dibromoarsine hydrobromide* at 145°, and the *diiodoarsine hydriodide* at 132° with decomposition.[481]

4-Diethylaminophenyldichloroarsine hydrochloride,

$$[HCl(C_2H_5)_2N]C_6H_4AsCl_2,$$

consists of snow-white needles, m. p. 139°; extremely soluble in water, sparingly in concentrated hydrochloric acid.[482]

4-Dimethylamino-2-methylphenyldichloroarsine hydrochloride,

$$[HCl(CH_3)_2N]C_6H_3(CH_3)AsCl_2,$$

melts at 112°.[483]

4-Dimethylamino-3-methylphenyldichloroarsine hydrochloride consists of needles, melting at 145°; has a pungent odor, is readily soluble in water or dilute hydrochloric acid and practically insoluble in the concentrated acid. The *dibromoarsine hydrobromide* forms rhombohedric plates, m. p. 168°, while the *diiodoarsine hydriodide* is a deep red crystalline powder.[484]

4 - Dimethylamino - 2,5 - dimethylphenyldichloroarsine hydrochloride, $[HCl(CH_3)_2N]C_6H_2(CH_3)_2.AsCl_2$, melts at 158°; the *dibromoarsine hydrobromide* at 160°.[485]

2-Dimethylamino-α-naphthyldichloroarsine hydrochloride,

$$[HCl(CH_3)_2N]C_{10}H_6AsCl_2,$$

melts at 158°; the *dibromoarsine hydrobromide* at 168°.[486]

4-Dimethylamino-α-naphthyldichloroarsine hydrochloride and the *dibromoarsine hydrobromide* are prepared like the previous compounds—from the arsineoxide and the respective haloid acid.[487]

2-Hydroxyphenyldichloroarsine, $HO.C_6H_4AsCl_2$. — Dry hydrogen chloride is conducted into a petroleum ether suspension of the anhydride of 2-hydroxyphenylarsineoxide, $C_6H_4 < \begin{matrix} As - O - As \\ | \qquad\quad | \\ O \qquad\quad O \end{matrix} > C_6H_4$, while warming and shaking, sulfur dioxide being also introduced to prevent oxidation. The resulting solution, after being dehydrated by means of calcium chloride and filtered while hot, deposits the dichloroarsine upon cooling in the form of flat, pale yellow, spear-shaped crystals. The yield may be increased by conducting more hydrogen chloride through the mother-liquor. It is possible that in the warm solution one molecule of hydrochloric acid splits off from the hydroxy dichloroarsine, leaving a compound, $C_6H_4 < \begin{matrix} AsCl \\ | \\ O \end{matrix}$, which upon further addition of hydrogen chloride is again converted into the dichloroarsine. The latter melts at 74-80°; is readily soluble in ether, benzene or carbon bisulfide, sparingly so in petroleum ether, and is easily hydrolyzed by water to the anhydride of 2-hydroxyphenylarsineoxide and hydrochloric acid.[488]

4-Methoxyphenyldichloroarsine, $(CH_3O)C_6H_4AsCl_2$, results when tri(4-methoxyphenyl)arsine is heated in a sealed tube with arsenic trichloride at 200° for 24 hours.[489] It may also be obtained by heating 4-methoxyphenylmercurichloride with arsenic trichloride on a water-bath for five hours.[490]

According to Michaelis and Weitz, the product is a colorless liquid, b. p. 230°/117 mm., while according to the later investigations of Goppelt[491] it solidifies on strong cooling to a colorless, crystalline mass, m. p. 48°; b. p. 160°/30 mm. With aqueous sodium hydroxide or carbonate solution it yields the corresponding arsineoxide. It readily absorbs chlorine in the cold, forming 4-methoxyphenylarsinetetrachloride. Hydrogen peroxide oxidizes a glacial acetic acid solution of the dichloroarsine to 4-methoxyphenylarsonic acid.

4-Methoxyphenyldiiodoarsine is obtained together with p-anisyltrimethylarsonium iodide on heating 4,4′-dimethoxyarsenobenzene with methyl iodide in a sealed tube at 100°.[492]

4-Ethoxyphenyldichloroarsine, $(C_2H_5O)C_6H_4AsCl_2$, is prepared by heating tri(4-ethoxyphenyl)arsine with arsenic trichloride at 220° for 24 hours. It is a colorless liquid, b. p. 198°/28 mm.; is converted into the arsineoxide by acqueous sodium carbonate; absorbs dry chlorine, forming the arsinetetrachloride; in the presence of water, however, the corresponding arsonic acid results.[493]

3-Amino-4-hydroxyphenyldichloroarsine hydrochloride,
$(HCl.H_2N)(HO)C_6H_3AsCl_2$,

may be obtained either from the corresponding arsineoxide and an excess of hydrochloric acid; [494] by adding a warm, aqueous mercuric chloride solution to an aqueous solution of arsphenamine, filtering off the mercurous chloride formed, and passing hydrogen chloride into the filtrate; [495] or by reducing the corresponding arsonic acid with sulfur dioxide in the presence of hydriodic acid at low temperature.[496] It crystallizes in colorless needles melting indefinitely at 200°, and decomposing when treated with mercuric chloride in alkaline solution. With cupric chloride in methyl alcoholic medium it forms a brown, amorphous coordination product easily soluble in water or sodium hydroxide.

4-Dimethylamino-3-methoxyphenyldichloroarsine hydrochloride,

$$[HCl(CH_3)_2N]C_6H_3(OCH_3)AsCl_2,$$

m. p. 152°, the corresponding *dibromoarsine hydrobromide,* and the *diiodoarsine hydriodide,* m. p. 92°, are prepared from the arsineoxide and the respective haloid acid.[497]

4-Carboxyphenyldichloroarsine (p-Benzarsenious chloride),

$$HOOC.C_6H_4AsCl_2,$$

is derived from the corresponding diiodoarsine by heating its ethereal solution with freshly prepared dry silver chloride in a sealed tube at 100°. A better procedure consists in treating 4-carboxyphenylarsonic acid with phosphorus trichloride at ordinary temperature:

$$HOOC.C_6H_4AsO(OH)_2 + 2PCl_3 \longrightarrow C_6H_4\begin{matrix} / AsCl_2 \\ \\ \backslash COCl \end{matrix} + POCl_3 + H_3PO_3.$$

The excess phosphorus trichloride is distilled off at 100°, the oily residue dissolved in benzene, and water cautiously added to decompose the phosphorus oxychloride. The benzene layer is then separated, dehydrated by means of calcium chloride and concentrated, the carboxyphenyldichloroarsine crystallizing out in colorless needles, m. p. 157-8°; decomposed upon boiling with water.[498]

According to Fourneau and Oechslin,[499] the above reaction does not yield $Cl_2As.C_6H_4.COCl$ as stated by LaCoste, but proceeds according to the equation:

$$HOOC.C_6H_4AsO(OH)_2 + PCl_3 \longrightarrow HOOC.C_6H_4AsCl_2 + HPO_3 + HCl.$$

4-Carboxyphenyldiiodoarsine, from the corresponding arsonic acid by warming with concentrated hydriodic acid containing a slight amount of red phosphorus, crystallizes from chloroform in yellow, felted needles,

m. p. 153° (LaCoste), 172° (Bertheim); readily soluble in alcohol or ether. It is partially decomposed by atmospheric moisture, more completely by boiling with water, into 4-carboxyphenylarsenious- and hydriodic acids.[500, 501]

4-Dichloroarsinobenzoyl chloride, $C_6H_4{<}\genfrac{}{}{0pt}{}{AsCl_2}{COCl}$.—To a chloroform solution of 4-carboxyphenylarsonic acid, a similar solution of phosphorus trichloride is slowly added and the reaction completed on a water-bath. After decanting from phosphoric acid, crystals of 4-carboxyphenyldichloroarsine separate, to which phosphorus pentachloride is immediately added, and the whole warmed for one hour. Finally, the chloroform and volatile chlorides of phosphorus are distilled off and the residue fractionated in vacuo. The same product is obtained by treating 4-carboxyphenylarsenious acid with either phosphorus tri- and pentachlorides successively, or with the latter alone; also by the action of phosphorus pentachloride upon 4-carboxyphenyldichloroarsine in chloroform solution.[502, 503]

The compound is a mobile liquid, fuming in moist air, b. p. 189-90°/19 mm.; soluble in chloroform, ether or benzene; yields a white precipitate with water; reacts like benzoyl chloride with alcohols, phenols, amino-alcohols, ammonia or alkaloids, such as quinine or morphine, which possess alcoholic or phenolic properties. With dimethylaminodimethylethylcarbinol in benzene solution it forms a condensation product, *dichloroarsinobenzoyldimethylaminodimethylethylcarbinol hydrochloride* (*4-Dichloroarsinostovaine*),

$$C_6H_4{<}\genfrac{}{}{0pt}{}{AsCl_2}{CO.O.C{\left\langle\begin{matrix}C_2H_5\\ CH_3\\ CH_2N(CH_3)_2.HCl.\end{matrix}\right.}}$$

This compound separates from absolute alcohol in white needles, m. p. 194°; readily soluble in water, sparingly in alcohol, insoluble in acetone. By treating its aqueous solution with soda and extracting with ether, the corresponding arsineoxide is obtained.[504]

4. *Aryl Arsineoxides and Dihydroxyarsines,* $RAsO$, $RAs(OH)_2$.—The unsubstituted oxides are readily obtained by treating the corresponding dihalogenated arsines with alkali hydroxides or carbonates:

$$RAsX_2 + Na_2CO_3 \longrightarrow RAsO + 2NaX + CO_2.$$

They form white, crystalline substances readily soluble in organic solvents, sparingly in alcohol, insoluble in water, and are unaffected by

the latter two solvents even on boiling. Haloid acids regenerate the dihalogenated arsines:

$$RAsO + 2HX \longrightarrow RAsX_2 + H_2O;$$

while heating above their melting points decomposes the compounds into tertiary arsines and arsenic trioxide:

$$3RAsO \longrightarrow R_3AsO + As_2O_3.$$

Oxidizing agents convert them into arsonic acids, and reducing agents to arseno compounds:

$$RAsO + O + H_2O \longrightarrow RAsO(OH)_2;$$
$$2RAsO + 2H_2 \longrightarrow RAs{=}AsR + 2H_2O.$$

The arsineoxides are amphoteric, dissolving in both concentrated acids and aqueous caustic alkalis, but only very sparingly in ammonia or alkali carbonates. With mercuric chloride in alkaline solution, replacement of the arsenic by mercury occurs, yielding either mercury diaryls or arylmercurichlorides and sodium arsenite.

Although unsubstituted aryl dihydroxyarsines or -arsenious acids corresponding to the formula $RAs(OH)_2$ have not as yet been isolated, various esters of phenylarsenious acid have been successfully obtained by the interaction of phenyldichloroarsine and sodium alcoholates or phenolates, except in the case of catechyl ester when the lead salt of catechol is employed:

$$C_6H_5AsCl_2 + 2RONa \longrightarrow C_6H_5As(OR)_2 + 2NaCl.$$

With the exception of the β-naphthyl and catechyl compounds, which are crystalline solids, the esters are all liquids distillable under diminished pressure, and are readily hydrolyzed by water or alkalis, yielding phenylarsineoxide and the corresponding alcohol or phenol:

$$C_6H_5As(OR)_2 + H_2O \longrightarrow C_6H_5AsO + 2ROH.$$

With chlorine or bromine decomposition occurs, except in the cases of the dimethyl and diethyl ester, which readily combine with chlorine to form additive compounds easily hydrolyzed by water or alcohol to phenylarsonic acid, the respetive alcohol and hydrochloric acid, e. g.,

$$\left\{\begin{array}{l} C_6H_5As(OCH_3)_2 + Cl_2 \longrightarrow C_6H_5As(OCH_3)_2.Cl_2 \\ C_6H_5As(OCH_3)_2.Cl_2 + 3H_2O \longrightarrow \\ \qquad C_6H_5AsO(OH)_2 + 2CH_3OH + 2HCl. \end{array}\right.$$

Substituted aryl arsineoxides may be prepared like the unsubstituted compounds from dihalogenated arsines. A more convenient method, however, consists in reducing the corresponding arsonic acids with either sulfurous acid (employing hydriodic acid as a catalyst), phenylhydrazine

or phosphorus trichloride in the presence of an indifferent diluent such as ether or ethyl acetate:

$$RAsO(OH)_2 + H_2 \longrightarrow RAsO + 2H_2O.$$

The reduction may be effected with sulfurous acid alone, but the process is very slow. If, however, a small amount of hydriodic acid is added the reaction proceeds very smoothly. The arsonic acid reacts with the hydriodic acid liberating free iodine:

$$RAsO(OH)_2 + 2HI \rightleftarrows RAsO + 2H_2O + I_2.$$

But oxidation of the arsineoxide to the arsonic acid by the liberated iodine is prevented by the sulfurous acid, which reduces the iodine to hydriodic acid, so that the above reduction is continuous, and enables a small amount of hydriodic acid to reduce large quantities of the arsonic acid.

The reduction by means of phosphorus trichloride in the presence of an indifferent diluent is of particular advantage in dealing with arsineoxides which are either decomposed by water or readily dissolved by it. But in those instances where the arsonic acid is only sparingly soluble in the solvent employed the reaction is incomplete, and the method unsatisfactory.

The presence of amino or substituted amino groups in the nucleus increases the reactivity and sensitivity of the arsineoxides to such an extent that their isolation in pure form is difficult. The hydrochlorides of N-alkylated aminoarylarsineoxides may be prepared directly from tertiary amines by heating with arsenic trichloride at water-bath temperature. The product is isolated by rendering alkaline, filtering and either acidifying the filtrate with hydrochloric acid and neutralizing with sodium carbonate or ammonia, or by adding a calculated quantity of ammonium chloride to the alkaline solution:

$$\begin{cases} R.N(R'R'') + AsCl_3 \longrightarrow [HCl.(R'R'')N]RAsCl_2 \\ HCl.(R'R'')N.RAsCl_2 + 3NaOH \longrightarrow \\ \qquad (R'R'')N.RAsO + 3NaCl + 2H_2O. \end{cases}$$

It is interesting to note that while unsubstituted aryl dihalogenated arsines react with alkalis yielding arsineoxides, the presence of nuclear nitro or carboxyl groups influences this reaction so that dihydroxyarsines (arsenious acids) result.

Phenylarsineoxide, C_6H_5AsO, is prepared from phenyldichloroarsine by treating its suspension in warm water with sodium carbonate, filtering, and recrystallizing the residual solid from hot alcohol. The arsineoxide separates in the form of colorless, crystalline crusts, m. p. 119-20°; slightly volatile in steam, and decomposing when heated above its melting point, yielding triphenylarsine and arsenic trioxide. At ordinary

temperature it has a characteristic anise-like odor, which upon warming becomes very irritating to the nasal mucous membrane. It is readily soluble in benzene, warm alcohol or caustic soda, sparingly in aqueous ammonia, insoluble in water, and is converted into the corresponding dichloroarsine when warmed with hydrochloric acid. An addition product, phenylarsineoxychloride, $C_6H_5AsOCl_2$, is obtained with chlorine, while with bromine the arsineoxide reacts vigorously, yielding the corresponding arsineoxybromide, together with bromobenzene and arsenic oxybromide:

$$2C_6H_5AsO + 2Br_2 \longrightarrow C_6H_5AsOBr_2 + C_6H_5Br + AsOBr.$$

Upon reduction, for example with phosphorous acid, sodium amalgam or zinc and hydrochloric acid, arsenobenzene is formed.[505, 506] When warmed with mercuric chloride in alkaline solution the arsenic is split off, yielding mercury diphenyl.[496]

Esters of Phenylarsenious Acid [Phenyldi(alkyl- or aryloxy) arsines].[507] — *Dimethylphenylarsenite,* $C_6H_5As(OCH_3)_2$. — From sodium methylate and phenyldichloroarsine in dry ethereal solution. It is a colorless liquid with a characteristic odor, b. p. 220° with partial decomposition, 116°/18 mm.; d, 1.343/20°; readily hydrolyzed by water or alkalis to phenylarsineoxide and methyl alcohol. It absorbs dry chlorine, forming colorless crystals of $C_6H_5As(OCH_3)_2Cl_2$, m. p. 90°; easily hydrolyzed by water or alcohol to phenylarsonic acid, methyl alcohol and hydrochloric acid:

$$C_6H_5As(OCH_3)_2Cl_2 + 3H_2O \longrightarrow C_6H_5AsO(OH)_2 + 2CH_3OH + 2HCl.$$

The ester forms no additive compound with bromine which decomposes it into phenylarsineoxybromide, methylene bromide, arsenic tribromide and dibromobenzene.

Diethylphenylarsenite, $C_6H_5As(OC_2H_5)_2$, prepared like the preceding ester employing sodium ethylate, is a colorless liquid with an unpleasant odor, b. p. 122°/15 mm. It is decomposed by bromine, but readily combines with chlorine, forming an oxychloride which consists of cubical crystals melting at 95°.

Diphenylphenylarsenite, $C_6H_5As(OC_6H_5)_2$, is obtained from sodium phenolate and phenyldichloroarsine, or by heating the latter with phenol at 200°. It is a colorless liquid becoming viscous but not solid when strongly cooled; b. p. 245°/15 mm.; d, 1.32/20°; readily hydrolyzed by moisture to phenylarsineoxide and phenol, and decomposed by chlorine or bromine thus:

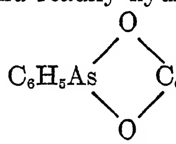
$$C_6H_5As(OC_6H_5)_2 + 8Cl_2 \longrightarrow C_6H_5AsCl_4 + 2C_6H_2Cl_3(OH) + 6HCl.$$

Di-p-cresylphenylarsenite, $C_6H_5As(OC_6H_4.CH_3)_2$, from the sodium salt of p-cresol and phenyldichloroarsine in xylene medium, is a pale yellow oil, b. p. 285°/12 mm.; d, 1.2989/13°.

Dibenzylphenylarsenite, $C_6H_5As(OCH_2C_6H_5)_2$, obtained like the preceding compound, is a pale yellow oil with an odor like benzyl alcohol, b. p. 296°/30 mm.; d, 1.2853/13°; decomposed in a similar manner by both chlorine and bromine, e. g.,

$$C_6H_5As(OCH_2C_6H_5)_2 + 5Cl_2 \longrightarrow$$
$$C_6H_4Cl_2 + 3HCl + AsCl_3 + C_6H_4Cl.COOH + C_6H_5CH_2Cl.$$

Di-β-naphthylphenylarsenite, $C_6H_5As(OC_{10}H_7)_2$, from sodium-β-naphthoxide and phenyldichloroarsine in ethereal solution, forms colorless needles melting at 113-4°, and readily hydrolyzed by water.

Catechylphenylarsenite, .—When phenyldichloroarsine is added to the lead salt of catechol suspended in xylene at ordinary temperature, a vigorous reaction occurs which is completed by heating in an oil-bath. The ester is obtained as a white crystalline mass, m. p. 83°; b. p. 197-8°/15 mm.; readily hydrolyzed by water. By the interaction of phenyldichloroarsine with the sodium salt of catechol, there is formed a solid containing chlorine and melting at 63°. It is probably a mixture of several distinct compounds.

2-Methylphenylarsineoxide, $(CH_3)C_6H_4AsO$.—Prepared from the corresponding dichloroarsine by boiling with concentrated sodium carbonate solution. It is a white powder, m. p. 145-6°; has a faint, not unpleasant aromatic odor; is sparingly soluble in caustic alkalis, and absorbs both chlorine and bromine, forming the respective oxyhalides, $C_7H_7AsOX_2$. When warmed with concentrated hydrochloric acid it is converted into the corresponding dichloroarsine.[449, 508]

3-Methylphenylarsineoxide, made like the preceding isomer, is a pasty, stringy mass. On warming its alcoholic solution with phosphorous acid, it is reduced to 3,3′-dimethylarsenobenzene.[509]

4-Methylphenylarsineoxide, m. p. 156°; possesses properties similar to those of its two isomers. When heated above its melting point it decomposes, yielding tri-(4-methylphenyl)arsine, while heating with an excess of phosphorous acid on a water-bath reduces it to the corresponding arseno compound. It absorbs both chlorine and bromine forming the corresponding oxyhalide.[449, 508, 452]

2,4-Dimethylphenylarsineoxide, $(CH_3)_2C_6H_3AsO$, is a viscous mass which can be obtained as a granular solid melting at 220° by permitting its alcoholic solution to drop into very cold water. It readily absorbs chlorine, forming an oxychloride—flat needles, m. p. 150°. By reduction with phosphorous acid the corresponding arseno compound is obtained, while with hydrogen sulfide in alcoholic solution it forms an arsinesulfide.[510]

2,5-Dimethylphenylarsineoxide, m. p. 165°, is reduced by phosphorous acid to the corresponding arseno compound.[457]

Tertiary-butylphenylarsineoxide, $(CH_3)_3C.C_6H_4AsO$, consists of a white crystalline powder, m. p. 89°, which is reduced by phosphorous acid to arseno tertiary-butylbenzene.[460]

α-Naphthylarsineoxide, $C_{10}H_7AsO$, exists as a white powder, m. p. 245°; sparingly soluble in boiling alcohol and insoluble in water, ether or benzene. Upon distillation it does not yield tri-α-naphthylarsineoxide, but decomposes into naphthalene, carbon and elemental arsenic.[511]

β-Naphthylarsineoxide, prepared by the action of alcoholic potash upon the corresponding dichloroarsine, is a white granular powder, m. p. 270°; sparingly soluble in alcohol, and practically insoluble in the usual solvents. It may be reduced by phosphorous acid to the arseno compound.[512]

4-Phenylphenylarsineoxide (Diphenyl-4-arsineoxide), $(C_6H_5)C_6H_4AsO$, melts at 198°.[513]

Anthraquinone-α-arsineoxide, $C_6H_4{\diagup CO \diagdown \atop \diagdown CO \diagup}C_6H_3AsO$, is formed on warming arsenoanthrahydroquinone in aqueous sodium carbonate. It is a dull yellow powder practically insoluble in the ordinary solvents, but soluble in concentrated sulfuric acid to a brownish-yellow solution. It is oxidized to the arsonic acid by hydrogen peroxide in hot alkaline medium, and reduced to arsenoanthrahydroquinone by sodium hydrosulfite.[514]

4-Chlorophenylarsineoxide, ClC_6H_4AsO, is made by reducing the corresponding arsonic acid with sulfur dioxide in the presence of hydriodic acid. On warming with mercuric chloride in alkaline solution, it yields mercury di(4-chlorobenzene).[496]

4-Iodophenylarsineoxide is obtained by the action of either water or alkali hydroxides or carbonates upon 4-iodophenyldiiodoarsine. It melts at 245-50°, and is soluble in all of the usual solvents except alcohol.[515]

3-Nitrophenyldihydroxyarsine (*3-Nitrophenylarsenious acid*),

$$(O_2N)C_6H_4As(OH)_2,$$

results upon dissolving the corresponding dichloro- or dibromoarsine in aqueous alkali, and precipitating either by a stream of carbon dioxide or by cautiously adding hydrochloric acid at low temperature. The dihydroxyarsine separates in white flakes readily soluble in alkali hydroxide solution or alcohol, less so in aqueous alkali carbonate and insoluble in water.[516]

4-Nitrophenylarsenious acid is prepared by reducing the corresponding arsonic acid with sulfur dioxide, using hydriodic acid as a catalyst. It is a powder insoluble in water but soluble in caustic soda from which, in contrast to the corresponding arsonic acid, it is reprecipitated by carbon dioxide.[86]

2,4-Dinitrophenylarsineoxide, $(O_2N)_2C_6H_4AsO$. — Phosphorus trichloride is gradually added to a suspension of 2,4-dinitrophenylarsonic acid in ether until the reaction and evolution of gas is completed, when the resulting ethereal solution is first washed with two volumes of water, then shaken with three volumes of same, and finally allowed to evaporate. The arsineoxide separates in yellow crusts soluble in alcohol or ether containing hydrochloric acid, with the formation of the corresponding dichloroarsine. It is also soluble in an excess of caustic soda but insoluble in water or dilute acids.[517]

2-Aminophenylarsineoxide, $(H_2N)C_6H_4AsO$.—A hydrochloric acid solution of the corresponding arsonic acid, to which a slight amount of potassium iodide has been added, is reduced with sulfur dioxide, and the aminophenylarsineoxide precipitated by neutralizing with alkali. It is a white powder readily soluble in aqueous caustic soda or dilute acids, and insoluble in sodium carbonate or ammonia. When allowed to stand for some time, it acquires a bluish tinge.[518]

4-Aminophenylarsineoxide.—p-Arsanilic acid, dissolved in dilute sulfuric acid to which a slight amount of potassium iodide has been added, is treated with sulfur dioxide at 20° for six hours, the whole then chilled to 5-10° and gradually rendered alkaline with concentrated ammonia while stirring vigorously. The crude product, which slowly precipitates, is purified by dissolving in dilute caustic soda, extracting with ether, and salting out by the addition of ammonium chloride solution to the aqueous layer.

The same compound results when a concentrated aqueous solution of atoxyl is acidified with hydrochloric acid, the precipitated sodium chloride filtered off, and the filtrate saturated with sulfur dioxide. After

twelve hours the hydrochloride of 4-aminophenyldichloroarsine begins to crystallize out. The solution is now saturated with hydrochloric acid, the above hydrochloride introduced into cold water, rendered alkaline with concentrated aqueous caustic soda, and the free arsineoxide salted out by saturating with sodium chloride.

It may also be obtained by boiling p-arsanilic acid with phenylhydrazine in methyl alcohol solution. After all of the nitrogen has been evolved, the alcohol is removed, the residual oily product mixed with dilute caustic soda and extracted with ether. Ammonium chloride is then added to the filtered aqueous layer and crystallization of the arsineoxide facilitated by scratching the walls of the vessel.

Another method of preparation consists in suspending p-arsanilic acid in dry ethyl acetate and adding phosphorus trichloride, whereupon a vigorous reaction ensues without producing a clear solution. After two hours absolute ether is added, the mixture allowed to stand for three more hours, and the precipitate, consisting of a mixture of unchanged arsonic acid and the hydrochloride of the corresponding dichloroarsine, is filtered off. From this the arsineoxide is obtained by dissolving in N-sodium hydroxide, filtering and adding ammonium chloride to the filtrate.[519]

The compound crystallizes with two molecules of water in well-defined, lustrous needles softening at 80°, and melting at 100° with foaming. The anhydrous compound softens at 90°, partially melts at 100°, and upon further heating, first resolidifies and then melts at 185-6°. It exhibits but feebly acidic properties, dissolving readily in caustic soda but not in sodium carbonate or ammonia. On the other hand, its basic properties are very pronounced, dissolving not only in dilute mineral acids but in aqueous acetic acid as well. It is readily soluble in hot water, cold methyl or ethyl alcohol, glacial acetic acid, acetone or pyridine, sparingly in cold water, ether or ethylacetate and insoluble in chloroform or benzene. When boiled with dilute hydrochloric acid it yields tri(4-aminophenyl)arsine and arsenic trioxide:

$$3(H_2N)C_6H_4AsO \longrightarrow (H_2N.C_6H_4)_3As + As_2O_3.$$

The arsineoxide readily reduces Fehling's solution or ammoniacal silver nitrate upon boiling, and is easily oxidized to the arsonic acid either by hydrogen peroxide in alkaline solution or by iodine in acetic acid solution. The latter is a quantitative reaction. It also behaves like an unsaturated compound, yielding 4-aminophenylarsinoacetic acid,

$$H_2N.C_6H_4As\begin{matrix} \diagup\!\!\!\diagup O \\ - OH \\ \diagdown CH_2COOH \end{matrix}$$

, with chloroacetic acid in alkaline solution.

Like all primary aromatic amines it can be diazotized and coupled with

various azo components, red dyes being obtained with R-salt or β-naphthoquinonesulfonic acid. It is decomposed by mercuric oxide in alkaline solution, yielding mercury dianiline.[496]

The arsineoxide is therapeutically more efficient than the arsonic acid, acting upon trypanosomes even in vitro, while the acid under such conditions remains inactive.

4-Amino-3-methylphenylarsineoxide, $H_2N.C_6H_3(CH_3)AsO$, prepared by reducing the corresponding arsonic acid with sulfur dioxide, consists of white crystals softening below 100° and melting at 160°; soluble in hot water, alcohol, acetone, dilute hydrochloric acid or caustic alkalis.[520]

4-Acetylaminophenylarsineoxide, $CH_3COHN.C_6H_4AsO$, exists in two forms: an indefinitely crystalline, anhydrous variety and a hydrous, crystalline modification. The first is prepared by reducing 4-acetylaminophenylarsonic acid with sulfurous acid, employing hydriodic acid as a catalyst. It melts at 288-9°, is soluble in caustic soda or hot 50 per cent acetic acid, sparingly in hot water or glacial acetic acid and insoluble in methyl or ethyl alcohol, sodium carbonate, ammonia or dilute mineral acids. The second variety, obtained by acetylating 4-aminophenylarsineoxide, forms wedge-shaped crystals containing one molecule of water and cannot be dehydrated or decomposed. At 100° it partially melts with foaming, then solidifies and finally remelts at 271°. When preserved in a desiccator for a long time it melts at 260° without exhibiting a preliminary melting point. It is readily soluble in hot water, methyl or ethyl alcohol, acetone, pyridine, glacial or 50 per cent acetic acid—the solutions occasionally exhibiting a turbidity due to the presence of a slight amount of the anhydrous variety—and is insoluble in ether, ethyl acetate or benzene. The crystalline product may be prepared from the anhydrous modification by dissolving in 2N-caustic soda solution, filtering into an excess of 2N-acetic acid and inducing crystallization by the addition of a few crystals of the desired product. Both varieties may be readily oxidized to the arsonic acid by means of dilute iodine in acetic acid solution.[521]

4-Carbethoxyaminophenylarsineoxide, $C_2H_5OOCHN.C_6H_4AsO$, results upon reducing the corresponding arsonic acid in dilute sulfuric acid solution with sulfur dioxide at 15°, employing hydriodic acid as a catalyst. It may also be obtained from the arsonic acid by suspending in ethyl acetate, chloroform or carbon tetrachloride and treating with phosphorus trichloride. The dichloroarsine, obtained as an intermediate product, is then dissolved in dilute caustic soda, and the arsineoxide precipitated by the addition of ammonium chloride solution or dilute acetic acid. A third method consists in dissolving one mole of 4-aminophenylarsineoxide in an equimolar amount of caustic soda, and gradually adding

to the well-cooled solution slightly more than one mole of ethyl chlorocarbonate. After standing for one hour the solution is acidified, and the precipitated product purified by dissolving in diluted alkali and reprecipitating with an acid.[522] It is a colorless, odorless powder soluble in hot water, glacial acetic acid, alcohol or dilute alkalis, sparingly in cold water and insoluble in sodium carbonate, chloroform, petroleum ether, carbon bisulfide, ether or benzene. Heated to 270°, it darkens and decomposes without melting. With hydrogen sulfide in alkaline solution, the oxygen of the arsineoxy group is replaced by one or more sulfur atoms.

Phenylglycine-4-arsineoxide, $(HOOCCH_2.HN)C_6H_4AsO$, is derived from the corresponding arsonic acid by reduction with sulfur dioxide in the usual manner.[523]

4-Methylaminophenylarsineoxide, $(CH_3.HN)C_6H_4AsO$, m. p. 65°, is made by heating a mixture of methylaniline and arsenic trichloride at water-bath temperature.[524]

4-Dimethylaminophenylarsineoxide, $(CH_3)_2N.C_6H_4AsO$, is a white powder, m. p. 75°; easily soluble in chloroform or hot alcohol and insoluble in water. It exhibits both basic and feebly acidic properties, dissolving in dilute acids and in an excess of concentrated sodium hydroxide solution.[525]

4-Diethylaminophenylarsineoxide, $(C_2H_5)_2N.C_6H_4AsO$, exists as a pale yellow powder, m. p. 58°; soluble in hot alcohol or dilute mineral acids.[526]

4-Dimethylamino-2-methylphenylarsineoxide,

$$(CH_3)_2N.C_6H_3(CH_3)AsO,$$

melts at 80°.[527]

4-Dimethylamino-3-methylphenylarsineoxide, from arsenic trichloride and dimethyl-o-toluidine at water-bath temperature,[528] is a white amorphous powder, m. p. 55°; readily soluble in alcohol, ether, chloroform or dilute acids but sparingly in water. Reduction with phosphorous acid in alcoholic solution converts it into the corresponding arseno compound, while oxidation with red mercuric oxide in aqueous suspension yields the arsonic acid.

4-Dimethylamino-2,5-dimethylphenylarsineoxide,

$$(CH_3)_2N.C_6H_2(CH_3)_2AsO,$$

melts at 95°.[529]

2-Dimethylamino-α-naphthylarsineoxide, $(CH_3)_2N.C_{10}H_6AsO$, melts at 128°,[530] and *4-dimethylamino-α-naphthylarsineoxide* at 125°.[531]

2-Chloro-4-methylaminophenylarsineoxide, $(CH_3HN)C_6H_3Cl.AsO$, obtained from 3-chloromethylaniline and arsenic trichloride, is a white, amorphous powder melting at 120°, decomposing at higher temperature and readily soluble in acetone, chloroform or alcohol.[532]

2-Chloro-4-dimethylaminophenylarsineoxide, $[(CH_3)_2N]C_6H_3Cl.AsO$, is a white powder, m. p. 88°; soluble in chloroform, benzene or dilute acids, insoluble in alcohol or ether. With concentrated hydrochloric acid it yields the hydrochloride of the corresponding dichloroarsine.[533]

2-Bromo-4-dimethylaminophenylarsineoxide melts at 92°.[534]

3-Nitro-4-aminophenylarsineoxide, $(O_2N)(H_2N)C_6H_3AsO$, obtained by reducing the corresponding arsonic acid, is a yellow powder soluble in alkalis to a brown-red solution.[535]

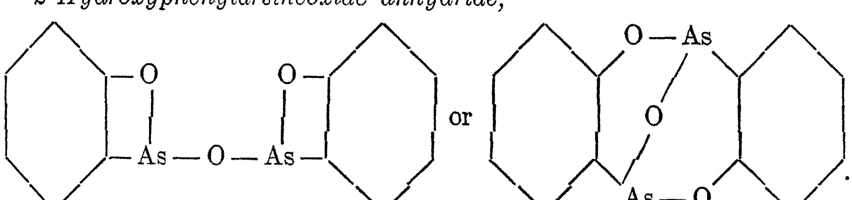
3-Nitro-4-triazophenylarsineoxide, $(O_2N)(N_3)C_6H_3AsO$, is made from 3-nitro-4-aminophenylarsonic acid by first converting it into its dichloroarsine with phosphorus trichloride, then diazotizing and treating with sodium azide. It is a colorless powder readily soluble in caustic soda, methyl or ethyl alcohol, but only sparingly so in sodium carbonate solution.[536]

3-Amino-4-carbethoxyaminophenylarsineoxide,

$$C_2H_5OOCHN.C_6H_3(NH_2)AsO.$$

Prepared from the corresponding arsonic acid in the same manner as 4-carbethoxyaminophenylarsineoxide. It is a slightly colored, amorphous powder without a definite melting point; readily soluble in glacial acetic acid, alcohol, or dilute acids and practically insoluble in the ordinary organic solvents. It dissolves readily in caustic alkalis, from which it is reprecipitated with difficulty.[322]

2-Hydroxyphenylarsineoxide anhydride,



Upon introducing a solution of 2-diazophenylarsonic acid into an equal volume of a cold saturated aqueous solution of sulfurous acid, there is

obtained a deep yellow liquid which is rapidly decolorized with a vigorous evolution of nitrogen, while the reaction product separates as a practically colorless powder. It crystallizes from hot glacial acetic acid in colorless, granular crystals, m. p. 177°; soluble in benzene, sparingly so in ether, and becoming dehydrated when dissolved in caustic soda solution. The above anhydride may also be made by hydrolyzing 2-hydroxyphenyldichloroarsine.[518]

4-Hydroxyphenylarsineoxide, $HO.C_6H_4AsO$.—Prepared by reducing the corresponding arsonic acid with sulfur dioxide in the presence of hydriodic acid. The resulting solution is saturated with sodium chloride, extracted with ether, and the ethereal extract, after neutralization with aqueous sodium carbonate solution, concentrated to crystallization. The same product may be obtained by employing other mild reducing agents such as phenylhydrazine, thionyl chloride or phosphorus trichloride.

The arsineoxide is a white, crystalline mass unaffected by heating up to 240°; readily soluble in water, methyl or ethyl alcohol, acetone, glacial acetic acid, or ethyl acetate and sparingly in benzene, chloroform or carbon bisulfide. When reduced with sodium hydrosulfite it is converted into 4,4′-dihydroxyarsenobenzene.[537]

4-Methoxyphenylarsineoxide, $CH_3O.C_6H_4AsO$, is a colorless crystalline mass obtained from the corresponding dichloroarsine by treatment with sodium hydroxide or carbonate.[489]

4-Ethoxyphenylarsineoxide, $C_2H_5O.C_6H_4AsO$, prepared like the previous compound, melts at 105°, and is readily reduced by phosphorous acid to the arseno compound.[493]

3,5-Dichloro-4-hydroxyphenylarsineoxide, $HO.C_6H_2Cl_2.AsO$, is made by reducing the arsonic acid. It crystallizes in small prisms sparingly soluble in water but readily so in alcohol, aqueous sodium hydroxide or carbonate.[538]

3-Nitro-4-hydroxyphenylarsineoxide, $(O_2N)(HO)C_6H_3AsO$, from the corresponding arsonic acid by reduction with sulfur dioxide, is a pale yellow powder decomposing upon heating; readily soluble in alkalis, glacial acetic acid, methyl or ethyl alcohol and sparingly in cold water.[539] It decomposes when warmed with mercuric chloride in alkaline solution, yielding mercurydi(3-nitro-4-hydroxybenzene).[496]

3-Amino-4-hydroxyphenylarsineoxide ["Arsenoxide"],

$$(H_2N)(HO)C_6H_3AsO.$$

To a solution of 46.8 g. of 3-amino-4-hydroxyphenylarsonic acid in 60 c.c. of water and 208 c.c. of hydrochloric acid (d, 1.12) there is added

10 g. of potassium iodide, and the whole saturated with sulfur dioxide at ordinary temperature. Concentrated ammonia is then gradually introduced at low temperature with continuous stirring until the whole assumes an alkaline reaction, and the arsineoxide completely precipitated by the addition of 220 g. of sodium chloride. From the impure product thus obtained, it is practically impossible to isolate the pure compound because of its sensitiveness and great solubility. It is readily soluble in water, mineral acids, methyl or ethyl alcohol, acetic acid, alkali hydroxides or carbonates but insoluble in absolute ether.[540] When boiled in acid solution it decomposes, yielding di(3-amino-4-hydroxyphenyl)-arsineoxide as an intermediate, and o-aminophenol as the final product.[541]

The *hydrochloride,* $(HCl.H_2N)(HO)C_6H_3AsO.\frac{1}{2}C_2H_5OH$, is readily obtained pure by dissolving the crude arsineoxide as completely as possible in absolute alcohol, filtering off inorganic impurities, adding absolute ether, refiltering and adding to the well-cooled filtrate a calculated amount of ethyl alcohol-hydrochloric acid drop by drop. The hydrochloride separates as a white pulverulent precipitate containing one half of a molecule of ethyl alcohol; is readily soluble in water, methyl or ethyl alcohol, sparingly in glacial acetic acid and practically insoluble in acetone or ether. The aqueous solution reacts neutral to congo but acid to litmus. It condenses with sodium-β-naphthoquinonesulfonate to a dark-red product soluble in alkalis, and also yields condensation products with phenol-aldehydes. In moist air the hydrochloride deliquesces, and after drying the molten mass to constant weight over calcium chloride contains one molecule of water instead of one half of a molecule of ethyl alcohol. Sodium hydrosulfite reduces it to 3,3′-diamino-4,4′-dihydroxyarsenobenzene, while with stannous chloride and an excess of hydrochloric acid the dihydrochloride of the same arseno compound is obtained.

4-Amino-3-hydroxyphenylarsineoxide, prepared from the corresponding arsonic acid like the previous compound, is a white powder readily soluble in acids or alkalis.[542]

4-Dimethylamino-3-methoxyphenylarsineoxide,

$$[(CH_3)_2N](CH_3O)C_6H_3AsO,$$

m. p. 60°, is obtained from 2-methoxydimethylaniline and arsenic trichloride by heating at water-bath temperature and treating the resulting dichloroarsine with caustic soda.[543]

5-Sulfo-3-amino-4-hydroxyphenyl-dihydroxyarsine or *-arsenious acid,* $(HO)_2As.C_6H_2(SO_3H)(OH)(NH_2)$.—On reducing 3-nitro-4-hydroxyphenylarsonic acid in dilute alkaline solution at $-2°$ with sodium hydrosulfite and allowing to stand over night at low temperature, crys-

tals of 3-amino-4-hydroxyphenylarsonic acid first separate. These are removed, the filtrate rendered slightly acid with concentrated hydrochloric acid and kept at 0° or below for one week, when a mixture of sodium sulfate, the above dihydroxyarsine and the corresponding arseno compound precipitates out. The sodium sulfate is first removed by water at 40°, the remaining solid dissolved in ammonia and the calcium salt of the arseno compound precipitated by the addition of a 4 per cent solution of calcium chloride. The dihydroxyarsine is then precipitated from the filtrate upon acidification with hydrochloric acid. The same product is also obtained upon reducing the corresponding arsonic acid with sulfur dioxide in the presence of hydriodic acid. It crystallizes in white, minute, elongated plates remaining unmelted up to 280°, practically insoluble in water and entirely so in acids. Its sulfur is not removed by heating with lead acetate in alkaline solution, and it is remarkably stable to hot dilute aqueous caustic soda. Its ammoniacal solution, in contrast to that of the corresponding arsonic acid, gives no precipitate with lithium chloride, calcium chloride or magnesia mixture either in the cold or hot; but forms a crystalline precipitate immediately upon the addition of barium chloride at room temperature. The dihydroxyarsine rapidly reduces ammoniacal silver nitrate solution to the metal in the cold. It can be readily diazotized and coupled with alkaline β-naphthol, yielding a deep reddish-brown, soluble dye.[544]

4-Carboxyphenyldihydroxyarsine (*4-Carboxyphenylarsenious acid, p-Benzarsenious acid*), $HOOC.C_6H_4As(OH)_2$.—Upon the addition of 4-carboxyphenyldiiodoarsine to an aqueous solution of sodium carbonate an evolution of carbon dioxide occurs, and a crystalline precipitate of the dihydroxyarsine is obtained upon acidulating with dilute hydrochloric acid. When recrystallized from hot water, it separates in colorless needles which lose $1H_2O$ at 145-160° and are converted into *4-carboxyphenylarsineoxide.* The latter consists of needles which do not melt up to 280°. The dihydroxyarsine is readily soluble in alcohol or warm water, and remains unaffected on prolonged boiling with concentrated hydrochloric acid, in contrast to phenyl- and the three methylphenylarsineoxides which yield the corresponding dichloroarsines. Upon boiling the free acid in water with calcium carbonate and concentrating the filtrate, a calcium salt, $[(HO)_2As.C_6H_4COO]_2Ca$, separates in iridescent leaflets sparingly soluble in hot water and losing $1H_2O$ above 100°, forming the salt, $(OAs.C_6H_4COO)_2Ca$. With silver nitrate it yields a white precipitate of the corresponding silver salt.[545]

The *ethyl ester of 4-carboxyphenylarsineoxide*, $C_2H_5OOC.C_6H_4AsO$, is prepared by dissolving dichloroarsinobenzoyl chloride in absolute alcohol and precipitating with dilute sodium carbonate solution. It is an amorphous powder, m. p. 277°; insoluble in water, sparingly soluble in alcohol and readily so in hot amyl alcohol. Caustic soda solution

readily hydrolyzes it to 4-carboxyphenylarsineoxide.[499] The *myricyl ester,* $C_{30}H_{61}OOC.C_6H_4AsO$, results upon the addition of a benzene solution of myricyl alcohol to 4-dichloroarsinobenzoyl chloride in the presence of pyridine. It separates from alcohol in white scales sparingly soluble in ether or hydrocarbons and insoluble in water or caustic alkalis. The *cholesterin ester,* $C_{27}H_{44}OOC.C_6H_4AsO$, consists of white flakes, and is prepared like the myricyl ester.[106] The *guaiacol ester,*

$$C_6H_4\begin{cases} AsO \\ CO.O.C_6H_4OCH_3 \end{cases}$$

, is made from 4-dichloroarsinobenzoyl chloride and guaiacol in benzene solution. It crystallizes from acetone-ether in tufts of small, white needles soluble in acetone or alcohol, insoluble in water or ether, and melting at 191°. It may be oxidized to the corresponding arsonic acid by means of hydrogen peroxide in acetone solution.[546] The *ester* with *dimethylaminodimethylethylcarbinol* (*4-Arsinoxystovaine*),

$$C_6H_4\begin{cases} AsO \\ CO.O.C\begin{cases} CH_2N(CH_3)_2 \\ CH_3 \\ C_2H_5 \end{cases} \end{cases}$$

, is obtained by the action of sodium carbonate upon the corresponding dichloroarsine. It is a viscous oil whose hydrochloride has a similar consistency.[499]

4-Amino-3-carboxyphenylarsineoxide, $(H_2N)(HOOC)C_6H_3AsO$, is obtained from the corresponding arsonic acid by reduction with sodium amalgam. It forms a black gold compound with auric chloride solution.[494]

4-Acetylamino-3-carboxyphenylarsineoxide,

$$(CH_3COHN)(HOOC)C_6H_3AsO,$$

is produced from 3-methyl-4-acetylaminophenylarsonic acid by boiling with phenylhydrazine in methyl alcohol solution, distilling off the greater part of the solvent and dissolving the residue in water. The excess phenylhydrazine is removed with ether, and the remaining aqueous solution concentrated in vacuo at 30-40°. The residue is then saturated with sodium chloride and acidified with dilute sulfuric acid at low temperature, the desired arsineoxide separating as a white powder decomposing at 300°; readily soluble in alkaline hydroxide or carbonate solutions, and in hot dilute hydrochloric acid, sparingly so in glacial acetic acid or hot water and insoluble in alcohol or ether.[520]

4-Arsinoxybenzoylglycine, $C_6H_4\genfrac{}{}{0pt}{}{\diagup AsO}{\diagdown CONHCH_2COOH}$. — From 4-dichloroarsinobenzoyl chloride by treatment with an alkaline solution of aminoacetic acid.[547]

4-Arsinoxybenzoylalanine, $C_6H_4\genfrac{}{}{0pt}{}{\diagup AsO}{\diagdown CONHCH(CH_3)COOH}$, is a white amorphous powder obtained from 4-dichloroarsinobenzoyl chloride by treating alanine in the presence of sodium bicarbonate. It is readily soluble in alkalis or alcohol, sparingly so in ether and insoluble in water.[106]

4-Arsinoxybenzoylphenylalanine,

$$C_6H_4\genfrac{}{}{0pt}{}{\diagup AsO}{\diagdown CONHCH(CH_2.C_6H_5)COOH},$$

is prepared like the alanine derivative.

4-Arsinoxybenzoylleucine, $C_6H_4\genfrac{}{}{0pt}{}{\diagup AsO}{\diagdown CONHCH[CH_2.CH(CH_3)_2]COOH}$, is obtained as above.

4-Arsinoxybenzoylaspartic acid, $C_6H_4\genfrac{}{}{0pt}{}{\diagup AsO}{\diagdown CONHCH(CH_2COOH)COOH}$, is slightly soluble in cold water.

4-Arsinoxybenzoylglutamic acid,

$$C_6H_4\genfrac{}{}{0pt}{}{\diagup AsO}{\diagdown CONHCH(CH_2.CH_2COOH)COOH},$$

changes into a glassy mass on continued standing in air.

4-Arsinoxybenzoyltyrosine, $C_6H_4\genfrac{}{}{0pt}{}{\diagup AsO}{\diagdown CONHCH(CH_2.C_6H_4OH)COOH}$,

prepared from 4-dichloroarsinobenzoyl chloride and tyrosine in the presence of an excess of caustic soda, is a white amorphous powder soluble in alcohol or alkalis, and only very sparingly in water.

N,N′-Pentamethylenebis(p-arsinosobenzamide),

$$C_6H_4\begin{array}{l} \diagup AsO \qquad\qquad OAs \diagdown \\ \diagdown CONH(CH_2)_5NHOC \diagup \end{array}C_6H_4,$$

resulting from the interaction of 4-dichloroarsinobenzoyl chloride and pentamethylenediamine in the presence of an excess of caustic soda, is a white powder soluble in caustic soda solution but insoluble in the usual solvents.[106]

4-Arsinoxybenzophenone (Benzophenone-4-arsineoxide),

$$C_6H_4\begin{array}{l} \diagup AsO \\ \diagdown COC_6H_5. \end{array}$$

A solution of 4-dichloroarsinobenzoyl chloride (20 g.) in dry carbon bisulfide (100 c.c.) is added to 25 c.c. of dry benzene, and 25 g. of anhydrous aluminium chloride introduced in 5 g. portions to reduce the intensity of the reaction. After refluxing on a water-bath at 50° for two hours, the warm reaction-mixture is poured upon 300 g. of cracked ice, 10 c.c. of concentrated hydrochloric acid is added, and the carbon bisulfide and excess benzene removed by steam distillation. The aqueous layer is then removed, and the remaining gummy mass warmed with 400 c.c. of dilute sodium carbonate and 50 c.c. of 6N-sodium hydroxide until practically complete solution is effected. After filtering and cooling, the arsineoxide is precipitated by dilute hydrochloric acid. It is an amorphous solid readily soluble in warm alkalis, sparingly in absolute alcohol, benzene, ether or boiling water. Hydrogen peroxide in alkaline solution oxidizes it to the corresponding arsonic acid.[548]

4-Dihydroxyarsinobenzophenone (Benzophenone-4-arsenious acid),

$$C_6H_4\begin{array}{l} \diagup As(OH)_2 \\ \diagdown COC_6H_5 \end{array}$$

, prepared by boiling the arsineoxide with water, is a crystalline solid readily soluble in alkalis, sparingly in absolute alcohol, and insoluble in ether or benzene.[548]

4-Arsinoxy-4′-methylbenzophenone, $C_6H_4 \begin{matrix} \diagup AsO \\ \diagdown COC_6H_4.CH_3 \end{matrix}$, from 4-dichloroarsinobenzoyl chloride and toluene, is difficult to obtain in the pure state on account of its amorphous character.[549]

4 - Dihydroxyarsino - 4′ - methylbenzophenone, $C_6H_4 \begin{matrix} \diagup As(OH)_2 \\ \diagdown COC_6H_4.CH_3 \end{matrix}$, consists of fine needles soluble in alkalis, sparingly so in ethyl alcohol and insoluble in ether or benzene. It is obtained from the arsineoxide by boiling with water.[549]

4-Arsinoxyphenylthioglycollic acid, $C_6H_4 \begin{matrix} \diagup AsO \\ \diagdown S.CH_2COOH \end{matrix}$, results upon reducing the corresponding arsonic acid with phenylhydrazine in methyl alcoholic solution.[550]

5. *Aryl Arsinesulfides and -Sesquisulfides*, RAsS and $R_2As_2S_3$.—The unsubstituted aromatic arsinesulfides are crystalline solids generally soluble in benzene or chloroform and only sparingly so in alcohol or ether. The most convenient method of preparation depends upon the interaction of hydrogen sulfide with the corresponding arsineoxide or dichloroarsine, generally in alcoholic solution:

$$RAsO + H_2S \longrightarrow RAsS + H_2O$$
$$RAsCl_2 + H_2S \longrightarrow RAsS + 2HCl.$$

The same compounds are also obtained by the addition of two atoms of sulfur to one molecule of an arseno compound:

$$RAs = AsR + S_2 \longrightarrow 2RAsS.$$

Nuclear substituted arsinesulfides are not only obtainable by the above methods, but in addition may be prepared by the action of hydrogen sulfide upon the corresponding arsonic acids:

$$RAsO(OH)_2 + 2H_2S \longrightarrow RAsS + S + 3H_2O.$$

In several instances boiling with hydrochloric acid converts the arsinesulfides into the corresponding dichloroarsines with evolution of hydrogen sulfide. They form sulfo salts with either alkali polysulfides or alkali sulfides and sulfur:

$$RAsS + Me_2S + S \longrightarrow RAsS(SMe)_2, \text{ (Me = an alkali metal).}$$

The primary aryl arsinesesquisulfides are generally derived fı arsonic acids by treating with hydrogen sulfide in alkaline solution, ε subsequently acidifying with hydrochloric acid. The reactions invol are:

$$\begin{cases} RAsO(OMe)_2 + 3H_2S \longrightarrow RAsS(SMe)_2 + 3H_2O \\ 2RAsS(SMe)_2 + 4HCl \longrightarrow R_2As_2S_3 + 2H_2S + S + 4MeCl. \end{cases}$$

The products are well-defined, crystalline substances usually soluble alkalis or organic solvents. They also dissolve in alkali polysulfic forming sulfo salts:

$$R_2As_2S_3 + Me_2S_2 + Me_2S \longrightarrow 2RAsS(SMe)_2.$$

The nuclear substituted compounds combine the properties of the sul derivatives and those of the corresponding non-arsenated organic cc pounds.

Phenylarsinesulfide, C_6H_5AsS, is prepared by saturating a dil alcoholic solution of the corresponding arsineoxide or dichloroarsine w hydrogen sulfide,[551] or by heating one mole of arsenobenzene with t atomic equivalents of sulfur.[552] It crystallizes from benzene in wh felted needles melting at 152°, and readily soluble in carbon bisulfi hot benzene or caustic soda. It also dissolves in yellow ammonium s fide, the resulting solution yielding the corresponding arsinesesquisulf with acids. The sulfide is difficultly soluble in alcohol, ether, ammor cold benzene or colorless ammonium sulfide; is unaffected by hyd chloric acid but oxidized to phenylarsonic acid by nitric acid. W mercury diethyl it forms phenyldiethylarsine:

$$C_6H_5AsS + Hg(C_2H_5)_2 \longrightarrow C_6H_5(C_2H_5)_2As + HgS.$$

Heated above its melting point in an atmosphere of carbon dioxide, ı sulfide decomposes in a similar manner as the arsineoxide, yielding t phenylarsine and arsenic trisulfide:

$$3C_6H_5AsS \longrightarrow (C_6H_5)_3As + As_2S_3.$$

4-Methylphenylarsinesulfide, $(CH_3)C_6H_4AsS$, consists of lustrı white crystals, m. p. 146°; readily soluble in benzene or chloroform a practically insoluble in alcohol or ether.[553]

2,4-Dimethylphenylarsinesulfide, $(CH_3)_2C_6H_3AsS$, fine white need from ether or benzene-alcohol, m. p. 169°.[510]

2,5-Dimethylphenylarsinesulfide, yellow needles, m. p. 188°.[554]

Tertiary-butyphenylarsinesulfide, $(CH_3)_3C.C_6H_4AsS$, lustrous le lets, m. p. 292°.[461]

4-Phenylphenylarsinesulfide, $(C_6H_5)C_6H_4AsS$, m. p. 190°.[555]

3-Nitro-4-methylphenylarsinesulfide, $(O_2N)C_6H_3(CH_3)AsS$.—Hydrogen sulfide is introduced into an aqueous solution of the corresponding arsonic acid at 70° for two hours, the whole permitted to stand for twelve hours, again warmed to 70°, and treated with hydrogen sulfide as before. After repeating this procedure two more times, the resulting mixture of the arsinesulfide and sulfur is purified by the addition of ammonia, which dissolves the arsenical while the sulfur remains unaffected. After filtering, the solution is neutralized with hydrochloric acid, and the resulting precipitate further purified by dissolving in benzene and reprecipitating with alcohol. It forms yellow needles melting at 141-2° and deflagrating at higher temperatures; is readily soluble in benzene or caustic alkalis, sparingly in alcohol and insoluble in water or ether.[556]

3-Aminophenylarsinesulfide, $(H_2N)C_6H_4AsS$.—A concentrated ammoniacal solution of 3-nitrophenylarsonic acid is saturated with hydrogen sulfide, warmed on a water-bath for twelve hours, fresh ammonia added and the whole operation repeated. It is finally evaporated to dryness, the residue taken up with water, and the arsinesulfide dissolved by the addition of dilute hydrochloric acid. After filtering off the free sulfur, the solution is rendered ammoniacal, producing a white voluminous precipitate of the arsinesulfide.[557]

According to Michaelis, ammonium aminophenylthioarsonate is formed as an intermediate product which is decomposed by the hydrochloric acid yielding the arsinesulfide:

$$(H_2N)C_6H_4AsS(SNH_4)_2 + 2HCl \longrightarrow$$
$$(H_2N)C_6H_4AsS + S + H_2S + 2NH_4Cl.$$

Bertheim,[558] however, claims that in the above reduction a mixture of 3-aminophenylarsine mono- and di- sulfides are obtained.

The aminophenylarsinesulfide is a white, uncrystallizable powder softening at 182° and melting at 188° to a yellow liquid. It is readily soluble in dilute hydrochloric acid or concentrated alkalis, sparingly in dilute alkalis, insoluble in water or the usual organic solvents. It is very sparingly soluble in concentrated hydrochloric acid, forming a hydrochloride which yields a white amorphous precipitate of the sulfate with dilute sulfuric acid. When boiled with hydrochloric acid the sulfide is converted into the corresponding dichloroarsine and hydrogen sulfide.

4-Aminophenylarsinesulfide results when a dilute hydrochloric acid solution of p-arsanilic acid is saturated with hydrogen sulfide, and the resulting precipitate freed of sulfur by extraction with carbon bisulfide. The arsinesulfide may also be prepared by dissolving the corresponding

arsineoxide in methyl alcohol and introducing hydrogen sulfide into t cooled solution as long as a precipitate is produced. It is a yellowis white crystalline powder sintering at 165° and melting at 180°; read: soluble in aniline or pyridine, less so in acetone, sparingly in alcol and insoluble in glacial acetic acid, benzene, chloroform or carbon bisı fide. It readily dissolves in warm caustic soda, from which it is fi: reprecipitated and then redissolved by an excess of mineral acids, exce in the case of concentrated hydrochloric acid when a precipitate of t hydrochloride is obtained.[559]

4-Dimethylaminophenylarsinesulfide, $(CH_3)_2N.C_6H_4AsS$, wh needles from chloroform, m. p. 187°; insoluble in alkalis or hot wat and soluble in cold dilute hydrochloric acid. The latter solution deco: poses upon heating, yielding the hydrochloride of the correspondi dichloroarsine and hydrogen sulfide.[479]

4-Diethylaminophenylarsinesulfide, $(C_2H_5)_2N.C_6HAsS$, exists white needles, m. p. 155°; readily soluble in chloroform and insoluble alcohol.[482]

4-Dimethylamino-2-methylphenylarsinesulfide,

$$(CH_3)_2N.C_6H_3(CH_3)AsS,$$

melts at 168°.[560]

4-Dimethylamino-3-methylphenylarsinesulfide is a pale-yellow, cr talline powder, m. p. 65-7°; readily soluble in ether or chloroform, sp: ingly in alcohol.[561]

4-Dimethylamino-2,5-dimethylphenylarsinesulfide,

$$(CH_3)_2N.C_6H_2(CH_3)_2AsS,$$

melts at 162°.[531]

4-Dimethylamino-α-naphthylarsinesulfide, $(CH_3)_2N.C_{10}H_6A$ m. p. 148°.[487]

2-Bromo-4-dimethylaminophenylarsinesulfide, $(CH_3)_2N.C_6H_3Br.A$ m. p. 198°.[562]

3-Amino-4-hydroxyphenylarsinesulfide, $(H_2N)(HO)C_6H_3AsS$, is white powder resulting from the action of hydrogen sulfide upon 3-ami: 4-hydroxyphenylarsineoxide. With palladium chloride in methyl al holic medium it forms a brown, complex double-salt readily soluble water or caustic soda.[494]

4-Dimethylamino-3-methoxyphenylarsinesulfide,

$$[(CH_3)_2N](CH_3O)C_6H_3AsS,$$

m. p. 90°.[563]

Phenylarsinesesquisulfide, $(C_6H_5)_2As_2S_3$.—An ammoniacal solution of phenylarsonic acid is saturated with hydrogen sulfide and acidified with hydrochloric acid, the sesquisulfide separating as a yellow resinous mass which may be obtained crystalline from benzene.[564] The same product is formed by dissolving the arsinesulfide in yellow ammonium sulfide and reprecipitating with acids. Another method of preparation consists in heating one mole of arsenobenzene and two atomic equivalents of sulfur together with a freshly prepared solution of ammonium sulfide in a sealed tube.[551] The product crystallizes from benzene in pale yellow, transparent prisms, from glacial acetic acid in long, narrow leaflets, and from alcohol or ether in fine, white needles melting at 130° and decomposing at higher temperatures. It is readily soluble in benzene or carbon bisulfide, less so in boiling glacial acetic acid, sparingly in alcohol or ether, slightly in caustic soda, and practically insoluble in ammonia. The compound dissolves very easily in sodium polysulfide, forming sodium phenyltrithioarsonate, $C_6H_5AsS(SNa)_2$; is unaffected by hydrochloric but oxidized by nitric acid to phenylarsonic acid with separation of free sulfur.

4-Methylphenylarsinesesquisulfide, $(CH_3.C_6H_4)_2As_2S_3$, is prepared by saturating an ammoniacal solution of the corresponding arsonic acid with hydrogen sulfide. It forms white needles from benzene-alcohol, m. p. 119-20°; readily soluble in benzene or carbon bisulfide, sparingly in hot glacial acetic acid, alcohol or ether.[553]

3-Nitrophenylarsinesesquisulfide, $(O_2NC_6H_4)_2As_2S_3$.—An aqueous solution of 3-nitrophenylarsonic acid is saturated with hydrogen sulfide at 50-60°, allowed to stand for twelve hours, and the whole process repeated four times. Ammonia is then added to the turbid solution, free sulfur removed by filtration, and the filtrate acidified with mineral acid. The sesquisulfide separates as a yellow precipitate which may be obtained in the form of yellow crystals from benzene-alcohol. It melts at 119° and intumesces at higher temperatures; is readily soluble in alkalis or benzene, sparingly so in alcohol, chloroform or carbon bisulfide and insoluble in water, ether or ligroin. Oxidizing agents readily convert it into 3-nitrophenylarsonic acid.[565]

4-Acetylaminophenylarsinesesquisulfide, $(CH_3COHNC_6H_4)_2As_2S_3$, prepared by the action of hydrogen sulfide upon the corresponding arsonic acid in ammoniacal solution, forms lustrous needles from alcohol, m. p.

208°; is readily soluble in aniline or pyridine, less so in alcohol or glacial acetic acid and sparingly in toluene or chloroform.[559]

3-Nitro-4-hydroxyphenylarsinesesquisulfide,

$$[(O_2N)(HO)C_6H_3]_2As_2S_3,$$

is obtained by saturating a solution of the arsonic acid in caustic soda with hydrogen sulfide at ordinary temperature and acidifying with hydrochloric acid. It is purified by recrystallizing first from acetone-water and then from boiling xylene, the product separating in hard, warty aggregates of yellow crystals melting at 160° with decomposition, and dissolving in alkalis to a reddish-brown solution.[566]

3-Amino-4-hydroxyphenylarsinesesquisulfide,

$$[(H_2N)(HO)C_6H_3]_2As_2S_3,$$

derived from the arsonic acid by treatment with hydrogen sulfide in either acid or alkaline solution, is soluble in acids, alkalis or methyl alcohol, and is reprecipitated from the latter by means of ether. When boiled with lead acetate in alkaline solution it loses its sulfur.[566]

Bis {p-[(acetylmercapto)amino]phenylarsylene} trisulfide, [Bis(S-acetylhydrosulfaminophenyl)-4,4′-arsinesesquisulfide],

$$[(CH_3CO.S.NH)C_6H_4]_2As_2S_3,$$

is formed together with the corresponding arsinedisulfide from atoxyl and formaldehydesulfoxylate. It separates from pyridine upon the addition of methyl alcohol as a yellow, amorphous substance, melting at 159° with decomposition.[567]

Hydrochloride of *4-aminophenylarsineselenide,* $(HCl.H_2N)C_6H_4AsSe$, separates on passing hydrogen selenide through an alcoholic solution of the corresponding dichloroarsine[568] or arsineoxide.[569] It is an orange-yellow powder quite difficultly soluble in water or dilute hydrochloric acid.

By passing hydrogen telluride through an alcoholic solution of 4-aminophenyldichloroarsine hydrochloride, the corresponding *arsinetelluride,* $(HCL.H_2N)C_6H_4AsTe$, is obtained as a red-brown substance sparingly soluble in dilute hydrochloric acid.[568]

6. *Arseno Compounds,* $R.As=As.R.$—Of all organic arsenicals, the most interesting chemically and the most valuable therapeutically are those containing the characteristic group $—As=As—$ which is the exact analogue of the azo group, $—N=N—$. Unlike the latter, however, it is at best only weakly chromophoric; in addition, the arseno compounds are much less stable than the corresponding azo derivatives.

The older and most frequently used method of preparation consists in reducing the corresponding arsonic acids or arsineoxides with various reducing agents. As the acids contain pentavalent arsenic, the reduction to the arseno condition is more difficult than in the case of the arsineoxides, in which the element is already in the trivalent form. Compounds of the latter type can, therefore, be reduced at ordinary or slightly elevated temperatures, while the arsonic acids usually require prolonged digestion. The reagents commonly employed for trivalent compounds are phosphorous or hypophosphorous acid, stannous chloride and hydrochloric acid, sodium amalgam in methyl alcoholic medium, or sodium hydrosulfite in neutral solution. The same reagents may be used with arsonic acids; in the case of phosphorous acid, however, it is further necessary to heat under pressure; with stannous chloride and hydrochloric acid a catalyst such as hydriodic acid is required; while with sodium hydrosulfite reduction is complete only upon warming at moderate temperatures. With the latter reagent the reaction generally proceeds smoothly, but the final product is often contaminated with impurities derived either from the reagent itself or formed as a result of a side-reaction. This is especially true in the case of 3-nitro-4-hydroxy-phenylarsonic acid, the resulting arsphenamine base being contaminated with more or less of an unidentified sulfur-containing arsenical. It has been claimed that the formation of this impurity may be limited, but not entirely prevented, by the presence of certain salts such as magnesium chloride.

Within recent years another satisfactory method for the preparation of arseno compounds has been developed, depending upon the condensation of a primary arsine with an arsineoxide, dihydroxy- or dichloroarsine:

$$RAsH_2 + R'AsO \longrightarrow RAs = AsR' + H_2O$$
$$RAsH_2 + R'As(OH)_2 \longrightarrow RAs = AsR' + 2H_2O$$
$$RAsH_2 + R'AsCl_2 \longrightarrow RAs = AsR + 2HCl.$$

This method is not only very satisfactory for the synthesis of arseno compounds in general, but is especially adapted for the production of those derivatives which contain two different hydrocarbon residues, and are known as Unsymmetrical Arseno Compounds. The latter may also be prepared by reducing mixtures of (1) two arsonic acids, (2) two arsineoxides, (3) an arsonic acid and an arsineoxide, or by the interaction of two symmetrical arseno compounds in warm solution:

$$RAsO(OH)_2 + R'AsO(OH)_2 + 4H_2 \longrightarrow RAs = AsR' + 6H_2O$$
$$RAsO + R'AsO + 2H_2 \longrightarrow RAs = AsR' + 2H_2O$$
$$RAsO(OH)_2 + R'AsO + 3H_2 \longrightarrow RAs = AsR' + 4H_2O$$
$$RAs = AsR + R'As = AsR' \longrightarrow 2RAs = AsR'.$$

The unsubstituted derivatives are generally crystalline substances with definite melting points, and do not dissolve in water, acids or

alkalis. They are oxidized very slowly on exposure to air, but may be readily converted into arsonic acids by stronger oxidizing agents. When heated above their melting points the compounds decompose into triarylarsines and free arsenic according to the equation:

$$3RAs = AsR \longrightarrow 2R_3As + As_4.$$

They form coordination products with various metallic salts, and react with alkyl halides, yielding among other products arsonium mono- and trihalides. With sulfur, aryl arsinesulfides are usually obtained, while with chlorine the resulting products are either dichloroarsines or arsinetetrachlorides, depending upon the amount of halogen employed:

$$RAs = AsR + S_2 \longrightarrow 2RAsS$$
$$RAs = AsR + Cl_2 \longrightarrow 2RAsCl_2 \xrightarrow{2Cl_2} 2RAsCl_4.$$

The arseno m- and p-xylenes possess the singular property of combining additively with two atoms of iodine in alcoholic medium to form symm. dixylyldiiododiarsines:

$$(CH_3)_2C_6H_3As = AsC_6H_3(CH_3)_2 + I_2 \longrightarrow \begin{array}{c} (CH_3)_2C_6H_3\underset{\textstyle I}{\underset{|}{As}}-\underset{\textstyle I}{\underset{|}{As}}C_6H_3(CH_3)_2 \end{array}$$

The preparation of pure substituted arseno derivatives is generally attended with great difficulty, as in most cases they are amorphous products insoluble in water or the usual organic solvents. Although some compounds can be purified by dissolving in a solvent such as alcohol and reprecipitating with ether, no general procedure has thus far been developed, as the organic impurities seem to possess the same solubilities as the arseno compounds themselves. The substituted derivatives exhibit not only the characteristic properties of an arseno compound, but also those of the corresponding substituted hydrocarbons. Thus, the arsenoarylamines form water-soluble salts with hydrochloric acid, insoluble sulfates with sulfuric acid, and condensation products with aldehydes, or salts such as sodium formaldehydesulfoxylate. Furthermore, the arylarseno phenols or carboxylic acids form soluble salts with alkalis, while those containing both acid and basic groups are amphoteric.

The introduction of substituents into the nuclei of arseno compounds increases their sensitiveness to oxygen to such an extent that on exposure to air they are oxidized more or less rapidly, depending upon the configuration of the individual molecule. The oxidation is more rapid in solution and even more so in the presence of alkalis, forming at first arsineoxides and finally arsonic acids. Furthermore, they readily reduce ammoniacal silver solutions and inorganic or organic mercurials to the metal, and are readily oxidized by nitric acid or iodine solution even at ordinary temperature.

Upon reducing a mixture of equimolar amounts of an organic arsine-

oxide or arsonic acid and an inorganic arsenic compound, there is obtained a product whose constitution probably corresponds to the formula,

$$\begin{array}{l} As = AsR. \\ | \\ As = AsR. \end{array}$$

The derivatives formed with proportionately larger quantities of the inorganic arsenical, however, contain more arsenic than that required by the above formula, and are also darker in color. The reaction may be carried out in the cold as well as at higher temperatures, depending upon the particular reducing agent selected. The products, which may also be prepared by passing arsine (AsH_3) through solutions of various dichloroarsines or arsineoxides, are generally yellow powders resembling the corresponding arseno compounds both with respect to their solubilities and reactions.

Similarly, by treating dichloroarsines or arsineoxides with phosphines or stibines, products called Arsenophosphides and -antimonides respectively are obtained. The latter may also be prepared by treating aromatic arylarsines with antimony trihalides or antimonous salts such as antimonyl chloride or tartar emetic:

$$RAsH_2 + SbX_3 \longrightarrow RAs = SbX + 2HX \quad (X = \text{a halogen atom});$$

by reducing mixtures of either arsineoxides or arsonic acids and stibonic acids by means of sodium hydrosulfite; or by condensing arsines with aryl stibineoxides or dihalogenated stibines.

The phosphides are generally yellow and the antimonides brownish amorphous substances possessing properties similar to those of the corresponding arseno compounds.

Finally, products containing bismuth attached to arsenic by a double link, and known as Arseno-bismuth compounds, have been prepared by condensing arylarsines with bismuth trihalides in methyl alcoholic solution containing the corresponding haloid acid. They are black amorphous products decomposing gradually when treated with acids or alkalis.

Arsenobenzene, $C_6H_5As = AsC_6H_5$, is prepared by reducing phenylarsineoxide or the corresponding arsonic acid with phosphorous acid.[31] In the latter case, the reduction may be more rapidly effected by employing hypophosphorous acid.[570] The product crystallizes in pale yellow needles melting at 196° (Michaelis), 208° (Binz), decomposing at higher temperature into triphenylarsine and free arsenic. It dissolves readily in carbon bisulfide, chloroform or benzene, forming solutions which readily resinify; is difficultly soluble in alcohol, and insoluble in water or ether. The arseno compound is converted into phenylarsonic acid by oxidizing agents, and combines directly with chlorine or sulfur, yielding phenyldichloroarsine and phenylarsinesulfide respectively. When

heated in a sealed tube with two atoms of sulfur in the presence of freshly prepared ammonium sulfide, it is partly converted into phenylarsinesesquisulfide. With mercury diethyl at 150°, phenyldiethylarsine is obtained:

$$(C_6H_5)_2As_2 + 2Hg(C_2H_5)_2 \longrightarrow 2C_6H_5(C_2H_5)_2As + Hg_2;$$

while with hydriodic acid at 100° for four hours, benzene, arsenic triodide and free arsenic are formed:

$$3(C_6H_5)_2As_2 + 6HI \longrightarrow 6C_6H_6 + 2AsI_3 + As_4.$$

The products obtained upon heating arsenobenzene with methyl iodide in a sealed tube at water-bath temperature, are phenyltrimethylarsonium iodide, -triiodide, and phenyldiiodoarsine;[571] with ethyl iodide, phenyltriethylarsonium iodide, phenyldiiodoarsine and symm. diphenyldiiododiarsine;[572] while with phenyltrimethylarsonium triiodide, the corresponding arsonium iodide and phenyldiiodoarsine are obtained.[200] By treating the arseno compound with silver nitrate in either pyridine or aqueous medium, there is formed a black coordination compound; with aqueous gold chloride a similar product is obtained; while a yellowish-brown coordination compound with cupric chloride results upon reducing a mixture of phenylarsonic acid and cupric chloride with hypophosphorous acid.[570, 573]

2,2′-Dimethylarsenobenzene (o-Arsenotoluene),

$$(H_3C)C_6H_4As = AsC_6H_4(CH_3),$$

is formed when the corresponding arsine oxidizes in air. It may be purified by crystallization from benzene and melts at 205-8°.[419]

3,3′-Dimethylarsenobenzene (m-Arsenotoluene) is a white amorphous powder, m. p. 106°, obtained by reducing the corresponding arsineoxide with phosphorous acid in alcoholic solution. It is insoluble in the usual organic solvents except carbon bisulfide or cymene.[509]

4,4′-Dimethylarsenobenzene (p-Arsenotoluene), prepared like its isomer, crystallizes in lustrous needles melting at 184°. Chlorine converts it successively into the dichloroarsine and arsinetetrachloride; nitric acid oxidizes it to p-tolylarsonic acid.[452] With methyliodide at 100°, it yields p-tolyltrimethylarsonium iodide and p-tolyldiiodoarsine.[574]

2,4,2′,4′-Tetramethylarsenobenzene (Arseno-m-xylene),

$$(CH_3)_2C_6H_3As = AsC_6H_3(CH_3)_2,$$

crystallizes from chloroform-ether in lustrous needles, m. p. 194-6°, and combines with iodine in alcoholic suspension to form symm. di-m xylyldiiododiarsine.[575]

2,5,2',5'-Tetramethylarsenobenzene (Arseno-p-xylene), is a white powder melting at 208°, and combining with iodine in alcoholic medium like its m-isomer.[457]

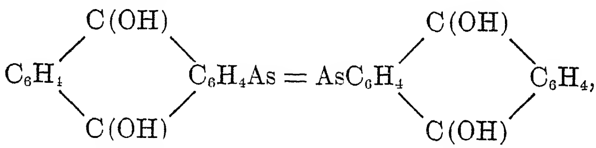
Di(tertiary-butyl)arsenobenzene, $(CH_3)_3CC_6H_4As{=}AsC_6H_4C(CH_3)_3$, melts at 198°.[460]

Arseno-α-naphthalene, $C_{10}H_7As = AsC_{10}H_7$, exists as yellow needles, m. p. 221°, sparingly soluble in alcohol, benzene, carbon bisulfide or chloroform, and insoluble in water or ether. It behaves in the usual manner with chlorine, sulfur or nitric acid. [443, 511]

Arseno-β-naphthalene separates from xylene as yellow needles, m. p. 234°.[576]

4,4'-Diphenylarsenobenzene, $(C_6H_5)C_6H_4As = AsC_6H_4(C_6H_5)$, is prepared by reducing the corresponding arsineoxide with phosphorous acid.[577]

Arsenoanthrahydroquinone,



obtained by reducing anthraquinonearsonic acid with sodium hydrosulfite, is a brown amorphous solid soluble in alcohol, ether or N-alkali, and insoluble in 2N-sodium carbonate. Its alkaline solution rapidly oxidizes to the parent arsonic acid on exposure to air.[578]

4,4'-Diiodoarsenobenzene, $IC_6H_4As = AsC_6H_4I$, is a yellow powder, insoluble in the usual organic solvents and melts at 145-50°. It is formed upon reducing the corresponding arsineoxide with phosphorous acid.[465] When heated with methyl iodide at 100°, it yields 4-iodophenyltrimethylarsonium iodide and 4-iodophenyldiiodoarsine.[574]

3,3'-Dinitroarsenobenzene, $(O_2N)C_6H_4As = AsC_6H_4(NO_2)$, results upon heating 3-nitrophenylarsonic acid with phosphorous acid in a sealed tube at 115° for 12 hours. It is a yellow, insoluble powder which intumesces without melting, forms additive compounds with halogens or sulfur, and is oxidized to the parent substance by nitric acid.[579]

3,3'-Dinitro-4,4'-dimethylarsenobenzene,

$$(O_2N)(H_3C)C_6H_3As = AsC_6H_3(CH_3)(NO_2),$$

similarly prepared, is a yellow powder decomposing at 165°, and insoluble in the usual solvents.[580]

?-Dinitro-2,5,2',5'-tetramethylarsenobenzene,

$$(O_2N)(H_3C)_2C_6H_2As = AsC_6H_2(CH_3)_2(NO_2),$$

is a yellow powder sintering at 165° and intumescing at higher temperatures. It is derived from the corresponding arsonic acid like the preceding compound.[554]

2,4,2',4'-Tetranitroarsenobenzene, $(O_2N)_2C_6H_3As = AsC_6H_3(NO_2)_2$.—From the corresponding arsonic acid by warming with hypophosphorous acid at 50-60° in the presence of a slight amount of hydriodic acid, and working up the resulting red-brown precipitate in an atmosphere of nitrogen or carbon dioxide. The product is soluble in the usual organic solvents.[469]

The following three arseno compounds, prepared by reducing the corresponding arsonic acids with boiling hypophosphorous acid, are soluble in alkalis, and yield the parent compounds upon oxidation with hydrogen peroxide:

3,3'-Bis(2-amino-3,6-disulfo-1-naphthylazo)arsenobenzene,

$$\begin{array}{l} AsC_6H_4.N = NC_{10}H_4(SO_3H)_2(NH_2) \\ \| \\ AsC_6H_4.N = NC_{10}H_4(SO_3H)_2(NH_2), \end{array}$$

a brownish-red powder; *4,4'-Bis(1-amino-8-hydroxy-3,6-disulfo-7-naphthylazo)arsenobenzene,*

$$\begin{array}{l} AsC_6H_4.N = NC_{10}H_3(SO_3H)_2(OH)(NH_2) \\ \| \\ AsC_6H_4.N = NC_{10}H_3(SO_3H)_2(OH)(NH_2), \end{array}$$

a dark powder with a metallic luster;[581] and *4,4'-Bis(2-amino-6-sulfo-8-hydroxy-1-naphthylazo)arsenobenzene,*

$$\begin{array}{l} AsC_6H_4.N = NC_{10}H_4(SO_3H)(OH)(NH_2) \\ \| \\ AsC_6H_4.N = NC_{10}H_4(SO_3H)(OH)(NH_2), \end{array}$$

a violet-red powder.[582]

2,2'-Diaminoarsenobenzene (o-Arsenoaniline),

$$(H_2N)C_6H_4As = AsC_6H_4(NH_2),$$

is a greenish-yellow powder produced by the electrolytic reduction of 2-nitrophenylarsonic acid in hydrochloric acid solution, and aerating the resulting liquid.[244]

4,4'-Diaminoarsenobenzene (p-Arsenoaniline) results upon reducing 4-aminophenylarsineoxide with sodium amalgam in methyl alcoholic solution,[583] with stannous chloride-hydrochloric acid,[584] or electrolytically

in an alkaline medium.[585] It may also be obtained from 4-aminophenylarsonic acid by treatment with sodium hydrosulfite at 50°,[586] by electrolysis in alkaline solution,[585] or by reduction with stannous chloride-hydrochloric acid,[587] especially in the presence of a slight amount of hydriodic acid.[588] The same product is precipitated upon condensing 4-aminophenylarsine with 4-aminophenylarsineoxide in hydrochloric acid solution and neutralizing with sodium acetate.[523]

The compound consists of pale-yellow flakes, m. p. 260°; soluble in pyridine, dilute hydrochloric acid, glacial or 50% acetic acid, and insoluble in water, aqueous alkalis or the usual organic solvents. Concentrated hydrochloric acid precipitates the hydrochloride from dilute acid solutions, while with dilute sulfuric acid an insoluble sulfate is obtained. The arseno compound possesses strong reducing powers, liberating the free metal from ammoniacal silver solution even in the cold. It is oxidized to p-arsanilic acid by hydrogen peroxide in alkaline or ammoniacal suspension, as well as by iodine in acetic acid solution. In addition, it exhibits the characteristic properties of a primary amine—it may be diazotized and coupled with azo components, and forms condensation products with aldehydes or β-naphthoquinonesulfonic acid. It also condenses with sodium benzaldehydebisulfite, forming a soluble product.[427]

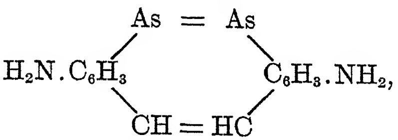
The dihydrochloride, $(HCl.H_2N)C_6H_4As = AsC_6H_4(NH_2.HCl)$, is a yellow crystalline powder, decomposing at 151° without melting; soluble in dilute hydrochloric acid, but insoluble in water or the usual organic solvents. The sulfate and the basic sulfite,

$$[H_2N.C_6H_4As = AsC_6H_4.NH_2]_2.H_2SO_3,$$

are also insoluble compounds, while the platinichloride is a yellowish-brown powder easily soluble in pyridine or dilute hydrochloric acid.[589]

4,4′-Diamino-α-arsenonaphthalene, $H_2N.C_{10}H_6As = AsC_{10}H_6.NH_2$, separates as a yellow insoluble dihydrochloride on reducing 4-nitro-α-naphthylarsonic acid with stannous chloride-hydrochloric acid in methyl aloholic solution. The free base, formed by hydrolyzing the above salt with water and 95% alcohol, has a reddish-brown color and, like its dihydrochloride, oxidizes very rapidly in moist air.[590]

5,5′-Diamino-1,1′-arseno-2,2′-stilbene,



is derived from 5,5′-diamino-2,2′-stilbenediarsonic acid by reduction with sodium hydrosulfite at 50-60° as a yellow precipitate insoluble in alkalis, and slightly soluble in excess of mineral acids.[591]

3,5,3′,5′-Tetranitro-4,4′-diaminoarsenobenzene,

$$(H_2N)(O_2N)_2C_6H_2As = AsC_6H_2(NO_2)_2(NH_2),$$

is a reddish-brown powder difficultly soluble in mineral acids and insoluble in alkalis or the usual organic solvents. It is prepared from 3,5-dinitro-4-aminophenylarsonic acid and phosphorous acid in alcoholic solution.[592]

2,4,2′,4′-Tetraaminoarsenobenzene, $(H_2N)_2C_6H_3As = AsC_6H_3(NH_2)_2$. —The corresponding arsonic acid is warmed to 70-80° with stannous chloride and hydrochloric acid containing a few drops of potassium iodide solution, cooled to 40°, and poured into glacial acetic acid. The resulting yellowish-white precipitate, consisting of a double chloride of the arseno compound and tin, is decomposed by dissolving in 2 to 3 N-hydrochloric acid, and adding successively glacial acetic acid and ether, the arseno compound separating as a yellowish-white precipitate. It is not only an extremely oxidizable compound, but is also readily hydrolyzed by water to m-phenylene diamine, arsenious and arsenic acids. It behaves like a meta diamine, coupling with diazo compounds to form azo dyes without loss of arsenic, and producing an azo-dye of the Bismarck-brown type with nitrous acid.[469]

3,4,3′,4′-Tetraaminoarsenobenzene results upon boiling 3-nitro-4-aminophenylarsonic acid with hypophosphorous acid in glacial acetic acid solution and finally adding potassium iodide.[593] With sodium formaldehydesulfoxylate it forms a condensation product which combines additively with cupric chloride to a yellowish-red powder soluble in alkalis.[594]

3,4,5,3′,4′,5′-Hexaaminoarsenobenzene,

$$(H_2N)_3C_6H_2As = AsC_6H_2(NH_2)_3,$$

may be prepared directly from 3,5-dinitro-4-aminophenylarsonic acid by reduction with either tin and hydrochloric acid[595] or sodium hydrosulfite,[596] or indirectly by first converting the above arsonic acid into 3,5,3′,5′-tetranitro-4,4′-diaminoarsenobenzene by means of phosphorous acid in alcoholic solution, and finally reducing with stannous chloride-concentrated hydrochloric acid.[592] The same product is also obtained on warming 3,4,5-triaminophenylarsonic acid with hypophosphorous acid.[592] The free base is a very unstable product, darkening rapidly on exposure to air. Its hydrochloride is a yellowish-green powder easily soluble in water or dilute acids, but insoluble in alkalis or the usual organic solvents. Upon adding aqueous sodium carbonate to a dilute hydrochloric acid solution of the salt, and thoroughly mixing the evolved carbon dioxide with the liquid, a precipitate of the free base is obtained which rapidly redissolves to a clear solution remaining unchanged upon

the addition of aqueous caustic soda. The solution is not very stable as the free base separates out within a very short time.[597] The hydrochloride yields an unsymmetrical arseno compound when warmed with either arsphenamine or bismethyl-3,4,5,3′,4′,5′-hexaaminoarsenobenzene hydrochloride.[598]

4,4′-Dioxalyldiaminoarsenobenzene,

$$HOOCCONH.C_6H_4As = AsC_6H_4.NHCOCOOH.$$

Obtained by reducing the corresponding arsonic acid with sodium hydrosulfite in sodium chloride solution at —15°, separating as a pale yellow precipitate insoluble in organic solvents, but soluble in alkalis. Upon warming its alkaline solution an insoluble compound is produced.[587]

4-Arsenophenylglycine,

$$HOOCCH_2HN.C_6H_4As = AsC_6H_4.NHCH_2COOH,$$

is a reddish-brown, readily oxidizable powder soluble in aqueous alkalis, aniline or pyridine, and insoluble in alcohol, ether, benzene or dilute mineral acids. It is obtained by warming the arsonic acid with sodium hydrosulfite which has been previously neutralized by the successive additions of dilute caustic soda and magnesium chloride.

The disodium salt,

$$NaOOCCH_2HN.C_6H_4As = AsC_6H_4.NHCH_2COONa,$$

[*"Spirarsen"*, *"Spirarsyl"*, "418" (in Ehrlich's series], produced from the acid derivative by dissolving in the requisite amount of concentrated sodium hydroxide solution and precipitating with alcohol, is a bright yellow, microcrystalline, water-soluble powder oxidizing in air to the corresponding arsineoxide.[587] It exhibits marked trypanocidal properties and has a comparatively low toxic action upon experimental animals, but the results obtained in human syphilis are not so favorable. This substance is of particular interest, as it was the first arseno compound whose biological behavior was so exhaustively studied by Ehrlich and his collaborators.[599]

A very stable derivative of 4-arsenophenylglycine is prepared by adding the requisite amount of 40% formaldehyde to its slightly alkaline solution, and precipitating with cold absolute alcohol.[600] With aqueous auric chloride the arseno compound forms a grayish-yellow addition product in which the gold is very firmly fixed. It is easily soluble in water or aqueous alkalis.[601]

4-Arseno-(2-methylphenylglycine), [p-Arseno-o-tolylglycine],

$$(HOOCCH_2NH)(H_3C)C_6H_3As = AsC_6H_3(CH_3)(NHCH_2COOH),$$

prepared like the preceding compound, is a yellowish-brown powder which darkens when heated above 200°, and is easily soluble in alkali

hydroxides or carbonates, sparingly so in the usual organic solvents except pyridine or aniline, and insoluble in water.[520]

3,5,3′,5′-Tetranitro-4,4′-bismethylaminoarsenobenzene,

$$[(H_3C)HN](O_2N)_2C_6H_2As = AsC_6H_2(NO_2)_2[NH(CH_3)],$$

is a slightly dark powder intumescing upon heating, readily soluble in acids, but insoluble in alkalis or the usual organic solvents. It results upon reducing the corresponding arsonic acid with phosphorous acid.[602]

3,5,3′,5′-Tetraamino-4,4′-bismethylaminoarsenobenzene, ["Arsalyt"],

$$[(H_3C)HN](H_2N)_2C_6H_2As = AsC_6H_2(NH_2)_2[NH(CH_3)],$$

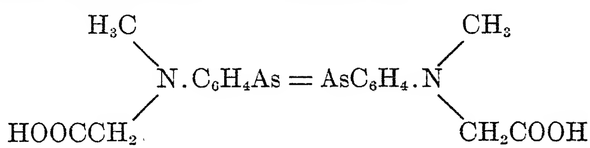
may be obtained from 3,5-dinitro-4-methylnitroaminophenylarsonic acid by reduction with either tin,[603] zinc dust or stannous chloride and hydrochloric acid,[604] or by hypophosphorous acid containing a slight amount of hydriodic acid;[605] from 3.5-dinitro-4-methylaminophenylarsonic acid by warming with sodium hydrosulfite; or by treating either 3,5,3′,5′-tetraaminoarsenophenylmethylhydrazine or 3.5,3′,5′-tetranitro-4,4′-bismethylaminoarsenobenzene, with tin and concentrated hydrochloric acid.[606] The free base is a yellowish-green powder, darkening on exposure to air, m. p. 95° with decomposition, readily soluble in acetone, acetic or hydrochloric acid, sparingly so in alcohol and insoluble in water. The hydrochloride is soluble in water, but insoluble in concentrated hydrochloric acid. A stable solution of the base is obtained by dissolving the hydrochloride in water and adding an excess of alkali bicarbonate either in vacuo or in an atmosphere of carbon dioxide.[607]

3,5,3′,5′-Tetraamino-4,4′-dipiperidinoarsenobenzene,

$$[(H_2C)_5N](H_2N)_2C_6H_2As = AsC_6H_2(NH_2)_2[N(CH_2)_5],$$

separates as a hydrochloride on treating the corresponding dinitroarsonic acid with stannous chloride and hydrochloric acid containing a few drops of potassium iodide solution. It is a yellow powder easily soluble in water, but insoluble in alkalis or organic solvents.[608]

p,p′-Arsenobis(N-methyl-N-phenylglycine),

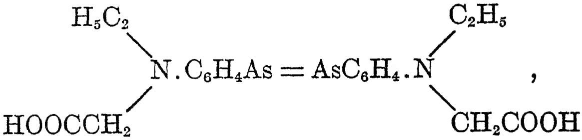


,

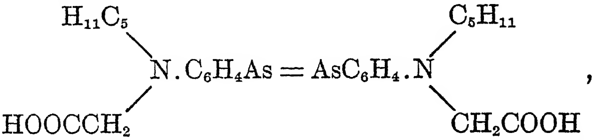
is a yellow powder soluble in alkali hydroxides or carbonates, but insoluble in acids or the ordinary organic solvents. It results upon reducing the corresponding arsonic acid with sodium hydrosulfite. From

its neutral solution in sodium hydroxide or carbonate, alcohol or acetone precipitates the bright-yellow, water-soluble sodium salt.[609]

p,p'-Arsenobis(N-ethyl-N-phenylglycine),

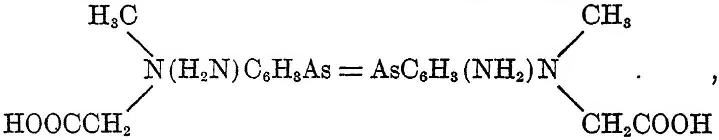


and the corresponding *amyl* compound,



resemble the methylglycine derivative both with regard to method of preparation and properties.[99]

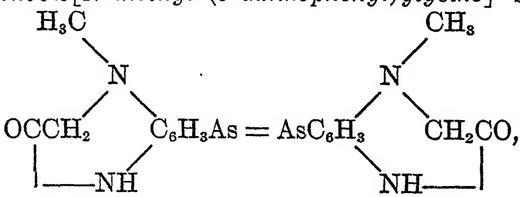
p,p'-Arsenobis[N-methyl-N-(2-aminophenyl)glycine],



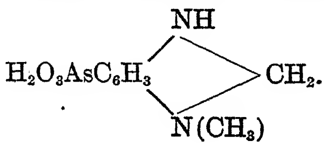
is obtained from the corresponding nitroarsonic acid by reducing with sodium hydrosulfite. Its disodium salt, which is very soluble in water but insoluble in organic solvents, can only be preserved in the dry state in vacuo.

The corresponding *ethyl* and *amyl glycine derivatives* resemble the methyl compound.[610]

p,p'-Arsenobis[N-methyl-(3-aminophenyl)glycine] separates as the anhydride,



on treating the corresponding nitroarsonic acid like the preceding compound.[610] It is insoluble in alkalis, acids or organic solvents. Upon oxidation with hydrogen peroxide, the following water-soluble acid is obtained,



p,p'-Arsenobis(N-acetyl-N-phenylglycine),

$$\begin{array}{ccc} CH_3CO & & COCH_3 \\ \diagdown & & \diagup \\ & N.C_6H_4As = AsC_6H_4.N & \\ \diagup & & \diagdown \\ HOOCCH_2 & & CH_2COOH \end{array},$$

obtained by treating the arsonic acid with sodium hydrosulfite, or by acetylating 4-arsenophenylglycine in sodium carbonate solution at 5° with the exclusion of air, is a yellow powder which is much more stable than 4-arsenophenylglycine.[611]

4,4'-Tetramethyldiaminoarsenobenzene,

$$(H_3C)_2N.C_6H_4As = AsC_6H_4.N(CH_3)_2,$$

from 4-dimethylaminophenylarsineoxide and sodium amalgam in alcoholic solution, is a yellow, granular, crystalline powder, m. p. 202°; readily soluble in chloroform or dilute acids, and insoluble in water or alcohol. It is easily oxidized to the parent compound when exposed to the air either in the dry state or in solution. Heated with concentrated hydrochloric acid in a sealed tube at 150°, it completely decomposes into dimethylaniline, arsenic trichloride and free arsenic:

$$3[(H_3C)_2N.C_6H_4As]_2 + 6HCl \longrightarrow 6C_6H_5.N(CH_3)_2 + 2AsCl_3 + As_4.$$

Its dihydrochloride is a red crystalline mass readily soluble in water, and rapidly oxidizing in air to the hydrochloride of the corresponding arsineoxide.[612]

4,4'-Tetraethyldiaminoarsenobenzene is a yellow, crystalline powder, m. p. 180°; readily soluble in chloroform or acids, but insoluble in alcohol. The hydrochloride is a red, crystalline, readily oxidizable salt.[482]

4,4'-Tetramethyldiamino-2,2'-dimethylarsenobenzene,

$$[(H_3C)_2N](H_3C)C_6H_3As = AsC_6H_3(CH_3)[N(CH_3)_2],$$

prepared from the arsineoxide like the two preceding compounds, melts at 155°.[560]

4,4'-Tetramethyldiamino-3,3'-dimethylarsenobenzene, is a stable, pale yellow powder, m. p. 75°; obtained from the arsineoxide by warming with phosphorous acid in alcoholic solution. The hydrochloride is a red hygroscopic mass.[561]

4,4'-Tetramethyldiaminoarsenonaphthalene,

$$(H_3C)_2N.C_{10}H_6As = AsC_{10}H_6.N(CH_3)_2,$$

m. p. 148°, is formed from the arsineoxide and sodium amalgam.[613]

3,3'-Diamino-4,4'-tetramethyldiaminoarsenobenzene,

$$[(H_3C)_2N](H_2N)C_6H_3As = AsC_6H_3(NH_2)[N(CH_3)_2],$$

consists of a yellow powder prepared from the corresponding nitrodimethylaminophenylarsonic acid and sodium hydrosulfite at 50-60°. Its tetrahydrochloride is a yellowish-white powder formed by dissolving the base in methyl alcoholic hydrochloric acid and precipitating with ether.[614]

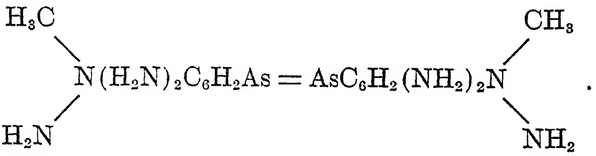
3,5,3',5'-Tetraamino-4,4'-tetramethyldiaminoarsenobenzene,

$$[(H_3C)_2N](H_2N)_2C_6H_2As = AsC_6H_2(NH_2)_2[N(CH_3)_2],$$

is isolated as the hydrochloride by reducing the corresponding dinitrodimethylaminophenylarsonic acid with stannous chloride and hydrochloric acid containing a few drops of potassium iodide solution. The salt is a yellowish-white powder easily soluble in water, more difficultly so in alcohol, and insoluble in alkalis or organic solvents.[608]

3,5,3',5'-Tetraamino-4,4'-tetraethyldiaminoarsenobenzene resembles the preceding compound with regard to properties and method of preparation.[608]

3,5,3',5'-Tetraaminoarsenophenylmethylhydrazine,



3,5-Dinitro-4-methylnitraminophenylarsonic acid is treated with stannous chloride and hydrochloric acid below 50°, and the arseno base precipitated by neutralization with caustic soda. It darkens in air, melts at 102-5° with decomposition, and is insoluble in water or the usual organic solvents. Its hydrochloride is a grayish-green powder, which also darkens in air, and is easily soluble in water or dilute acids, but insoluble in alkalis.[615]

3,5,3',5'-Tetraamino-2,4,2',4'-tetramethyltetraaminoarsenobenzene, $(H_3C.HN)_2(H_2N)_2C_6HAs = AsC_6H(NH_2)_2(NHCH_3)_2$, is obtained as a yellow hydrochloride upon reducing 4-methylnitramino-3,5-dinitro-2-methylaminophenylarsonic acid with tin and hydrochloric acid. Its dilute sodium carbonate solution remains stable for an indefinite period in an atmosphere of nitrogen or carbon dioxide.[616]

2,2'-Dibromo-4,4'-tetramethyldiaminoarsenobenzene,

$$[(H_3C)_2N]BrC_6H_3As = AsC_6H_3Br[N(CH_3)_2],$$

m. p. 235°, is formed from the corresponding arsineoxide and sodium amalgam.[617]

2,2'-Dichloro-3,5,3',5'-tetraamino-4,4'-bismethylaminoarsenobenzene, $[(H_3C)HN](H_2N)_2ClC_6HAs = AsC_6HCl(NH_2)_2[NH(CH_3)]$, prepared from 2-chloro-3,5-dinitro-4-methylnitraminophenylarsonic acid by reduction with zinc or tin and hydrochloric acid, rapidly darkens on exposure to the air, is soluble in dilute hydrochloric acid, and insoluble in water. It also dissolves in aqueous sodium bicarbonate, forming a yellow solution which is stable in an atmosphere of carbon dioxide.[616] The hydrochloride is a yellowish-green powder easily soluble in water, sodium carbonate or bicarbonate solution.[618]

2,6,2',6'-Tetrachloro-3,5,3',5'-tetraamino-4,4'-bismethylaminoarsenobenzene, $[(H_3C)HN](H_2N)_2Cl_2C_6As = AsC_6Cl_2(NH_2)_2[NH(CH_3)]$, is a yellow powder prepared like the preceding compound. It forms a stable solution with aqueous sodium or ammonium bicarbonate. The hydrochloride is soluble in water, while the sulfate is insoluble.[616]

2,2'-Dibromo-3,5,3',5'-tetraamino-4,4'-bismethylaminoarsenobenzene resembles the corresponding chlorine derivative both with regard to method of preparation and properties.[616, 618]

4,4'-Dihydroxyarsenobenzene (p-Arsenophenol),

$$HO.C_6H_4As = AsC_6H_4.OH.$$

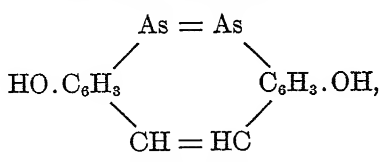
Obtained by reducing the corresponding arsineoxide,[619] or arsonic acid with sodium hydrosulfite.[620] It is a yellowish-brown powder decomposing above 200°; readily soluble in aqueous caustic soda, alcohol, acetone or ether, and insoluble in dilute mineral acids, benzene or chloroform. The disodium salt is a yellow powder readily soluble in water but only sparingly in methyl or ethyl alcohol. With auric chloride in concentrated aqueous solution, it forms a black addition product.[594]

4,4'-Dihydroxy-3,3'-dimethylarsenobenzene [p-Arseno-o-cresol],

$$(HO)(H_3C)C_6H_3As = AsC_6H_3(CH_3)(OH),$$

resembles the preceding compound both as to properties and method of preparation.[620]

5,5'-Dihydroxy-1,1'-arseno-2,2'-stilbene,



is formed by reducing the corresponding diarsonic acid with sodium hydrosulfite.[621]

4,4′-Dimethoxyarsenobenzene (p-Arsenoanisole),

$$CH_3O.C_6H_4As = AsC_6H_4.OCH_3,$$

obtained by treating the corresponding arsonic acid with aqueous phosphorous acid in a sealed tube at 100°, is a yellow powder, m. p. 200° with decomposition. With methyl iodide at 100°, it yields 4-methoxyphenyltrimethylarsonium iodide, and 4-methoxyphenyldiiodoarsine.[493]

4,4′-Diethoxyarsenobenzene (p-Arsenophenetole), from 4-ethoxyphenylarsineoxide and phosphorous acid, is a yellow powder which readily becomes resinous.[622]

p-Arsenophenylglycollic acid,

$$HOOCCH_2.O.C_6H_4As = AsC_6H_4.O.CH_2COOH,$$

is a yellow powder formed upon reducing the corresponding arsonic acid with sodium hydrosulfite. It reduces ammoniacal silver solution at ordinary temperature. The disodium salt is a yellow powder easily soluble in water but difficultly so in alcohol.[623]

p-Arsenophenylthioglycollic acid,

$$HOOCCH_2.S.C_6H_4As = AsC_6H_4.S.CH_2COOH,$$

is prepared in two stages: the corresponding arsonic acid is first converted into the arsineoxide by means of phenylhydrazine in methyl alcoholic solution, and the oxide in turn reduced with sodium amalgam. The free acid, as well as its disodium salt, behaves like the previous compound.[623]

3,3′-Dihydroxy-4,4′-dimethoxyarsenobenzene,

$$(CH_3O)(HO)C_6H_3As = AsC_6H_3(OH)(OCH_3),$$

separates as a colorless precipitate upon warming the corresponding arsonic acid with a dilute solution of hypophosphorous acid.[624]

4,4′-Dihydroxy-2,2′-dimethoxyarsenobenzene, similarly prepared, is a yellow powder readily soluble in aqueous sodium hydroxide, but insoluble in sodium carbonate.[625]

4,4′-Dihydroxy-3,3′-dimethoxyarsenobenzene, is a colorless precipitate.[626]

3,4,3′,4′-Tetramethoxyarsenobenzene,

$$(CH_3O)_2C_6H_3As = AsC_6H_3(OCH_3)_2,$$

is a white amorphous precipitate.[627]

3,5,3′,5′-Tetrachloro-4,4′-dihydroxyarsenobenzene,

$$(HO)Cl_2C_6H_2As = AsC_6H_2Cl_2(OH),$$

separates upon warming the corresponding arsonic acid with sodium hydrosulfite at 50° as a yellow powder soluble in alcohol, ether, alkali hydroxides or carbonates but insoluble in water.[628]

3,5,3′,5′-Tetrabromo-4,4′-dihydroxyarsenobenzene, similarly prepared,[628] is a yellow powder which is oxidized upon the addition of an excess of methyl alcoholic silver nitrate to its pyridine-methyl alcohol solution, yielding two compounds, one of which has been identified as a pyridine-silver arsonic acid derivative of the following composition,

$$\begin{array}{l} (3)\ Br \diagdown \\ (5)\ Br - C_6H_2AsO_3H_2.C_5H_5N, \\ (4)\ AgO \diagup \end{array}$$

m. p. 157-8°.[629] When aqueous silver nitrate (2 mols.) is added to a solution of the disodium salt of the arseno compound, a brown precipitate of the disilver salt,

$$AgO.C_6H_2Br_2As = AsC_6H_2Br_2.OAg,$$

is obtained.[570]

3,5,3′,5′-Tetraiodo-4,4′-dihydroxyarsenobenzene resembles the above two tetrahalogenated arsenophenols.[628]

3,3′-Dinitro-4,4′-dihydroxyarsenobenzene,

$$(O_2N)(HO)C_6H_3As = AsC_6H_3(NO_2)OH.$$

Prepared from 3-nitro-4-hydroxyphenyl arsonic acid or arsineoxide by reduction with either stannous chloride-hydrochloric acid containing a slight amount of hydriodic acid at low temperature, or with hypophosphorous acid in the absence of air at water-bath temperature.[630] It is a bright yellow powder which becomes electrified by friction, is soluble in alkali hydroxides or carbonates but only sparingly in excess of these reagents, very sparingly soluble in the usual organic solvents, and insoluble in water. The dry compound should be handled carefully, as it has a tendency to inflame spontaneously.

5,5′-Dinitro-3,3′-dihydroxy-4,4′-dimethoxyarsenobenzene,

$$\begin{array}{ccccc} HO & & & & OH \\ & \diagdown & & \diagup & \\ CH_3O - & C_6H_2As & = & AsC_6H_2 & - OCH_3. \\ & \diagup & & \diagdown & \\ O_2N & & & & NO_2 \end{array}$$

A bright yellow precipitate obtained by reducing the corresponding arsonic acid with hypophosphorous acid.[624]

5,5'-Dinitro-4,4'-dihydroxy-3,3'-dimethoxyarsenobenzene is similarly prepared.[631]

3,5,3',5'-Tetranitro-4,4'-dihydroxyarsenobenzene,

$$(O_2N)_2(HO)C_6H_2As = AsC_6H_2(OH)(NO_2)_2,$$

is a yellow powder resulting upon warming the corresponding arsonic acid with hypophosphorous acid in glacial acetic acid medium.[605]

4,4'-Dihydroxy-3,3'-bis(2''-hydroxynaphthaleneazo)arsenobenzene, $(HO.C_{10}H_6.N = N)(HO)C_6H_3As = AsC_6H_3(OH)(N = N.C_{10}H_6.OH)$, is a dark red powder prepared by boiling the corresponding arsonic acid with hypophosphorous acid.[582]

4,4'-Dihydroxy-3,3'-bis(2'',4'',6''-trihydroxy-1-azo)arsenobenzene, $[(HO)_3C_6H_2N = N](HO)C_6H_3As = AsC_6H_3(OH)[N = N.C_6H_2(OH)_3]$, is a red powder soluble in alkalis, and is oxidized by hydrogen peroxide to the parent compound. It is prepared like the preceding compound.[581]

3,5,3',5'-Tetraamino-4,4'-dihydroxyarsenobenzene,

$$(H_2N)_2(HO)C_6H_2As = AsC_6H_2(OH)(NH_2)_2,$$

is a pale yellow powder obtained from 3,5-dinitro-4-hydroxyphenylarsonic acid either by reducing with sodium hydrosulfite,[632] or by warming with hypophosphorous acid in the presence of glacial acetic acid, adding potassium iodide, and precipitating with sodium carbonate.[605] It darkens and decomposes at 155-7°, is easily soluble in alkalis or dilute hydrochloric acid, and insoluble in water or the usual organic solvents.

The tetrahydrochloride has been prepared by dissolving the base in dilute hydrochloric acid and precipitating with the concentrated acid;[605] or by introducing the base into methyl alcoholic hydrochloric acid, filtering and precipitating with ether.[633] According to Raiziss it appears to exist in two modifications—one easily soluble in methyl alcohol, and the other only sparingly so. Both products are yellow, amorphous substances easily soluble in cold water or caustic alkalis, and oxidizing more rapidly than arsphenamine on exposure to air, especially in alkaline solution. The base is gradually precipitated from the latter solution by atmospheric carbon dioxide.

5,5'-Diamino-2,4,2',4'-tetrahydroxyarsenobenzene,

$$(H_2N)(HO)_2C_6H_2As = AsC_6H_2(OH)_2(NH_2),$$

separates as a dihydrochloride upon gently warming 5-nitro-2,4-dihydroxyphenylarsonic acid with stannous chloride in alcoholic hydrochloric acid, adding glacial acetic acid, and gradually introducing the filtrate

with stirring into an ice-cold mixture of concentrated hydrochloric, glacial acetic, and a slight amount of hydriodic acids. The resulting yellow water-soluble precipitate, when treated with the proper amount of caustic soda, yields the free base which is soluble in excess of the reagent. The alkaline solution turns blue on exposure to air due to oxidation.[634]

3,5,3′,5′-Tetraamino-2,4,2′,4′-tetrahydroxyarsenobenzene,

$$(H_2N)_2(HO)_2C_6HAs = AsC_6H(OH)_2(NH_2)_2.$$

3,5-Dinitro-2,4-dihydroxyphenylarsonic acid is first reduced to the corresponding diamino compound by warming with stannous chloride and hydrochloric acid, a small quantity of potassium iodide added to the resulting solution, and the whole gradually introduced with stirring into ice-cold concentrated hydrochloric acid, the tetrahydrochloride of the above arseno compound separating as a fine yellow precipitate soluble in water or dilute hydrochloric acid. Upon boiling its aqueous solution, the arsenic is split off, yielding 2,4-diaminoresorcinol. From an aqueous solution of the tetrahydrochloride, caustic soda precipitates the free base which is soluble in excess of the reagent, as well as in sodium carbonate or bicarbonate. Its alkaline solution oxidizes in the air and turns blue due to the formation of an iodophenol dye. In mineral acid the arseno compound forms a light yellow diazo derivative, but in acetic acid it yields a deep-brown precipitate which is probably a dye of the Bismarck-brown type formed by the splitting off of arsenic from the molecule. A similar removal of arsenic occurs upon attempting to couple the arseno compound with diazo-p-nitroaniline in alkaline solution, a brownish-red dye resulting.[635]

3,3′-Diacetyldiamino-4,4′-dihydroxyarsenobenzene,

$$(CH_3CO.HN)(HO)C_6H_3As = AsC_6H_3(OH)(NH.COCH_3),$$

is a pale yellow powder obtained by reducing 3-acetylamino-4-hydroxyphenylarsonic acid with sodium hydrosulfite. It melts at about 200°, is soluble in acetone, aqueous sodium hydroxide or carbonate, difficultly so in alcohol and insoluble in water, methyl alcohol, ether, dilute acids or sodium bicarbonate.[636]

3,5,3′,5′-Tetraacetyltetraamino-4,4′-dihydroxyarsenobenzene,

$$(CH_3CO.HN)_2(HO)C_6H_2As = AsC_6H_2(OH)(NH.OCCH_3)_2,$$

obtained by reducing the corresponding arsonic acid with sodium hydrosulfite at 55-60°, is a white powder soluble in glacial acetic acid, aqueous caustic alkalis or sodium bicarbonate, and insoluble in water, dilute hydrochloric acid or the usual organic solvents.[637]

5,5′-Diacetyldiamino-2,4,2′,4′-tetrahydroxyarsenobenzene,

$$(CH_3CO.HN)(HO)_2C_6H_2As = AsC_6H_2(OH)_2(NH.OCCH_3).$$

A yellow powder insoluble in water, but readily soluble in aqueous caustic soda. It is derived from the corresponding arsonic acid by reduction with hypophosphorous acid containing a slight amount of hydriodic acid.[635]

3,5,3′,5′-Tetraacetyltetraamino-2,4,2′,4′-tetrahydroxyarsenobenzene, $(CH_3CO.HN)_2(HO)_2C_6HAs = AsC_6H(OH)_2(NH.COCH_3)_2$, is a brown powder, readily soluble in sodium carbonate or bicarbonate. It is prepared by acetylating 3,5,3′,5′-tetraamino-2,4,2′,4′-tetrahydroxyarsenobenzene with acetic anhydride.[635]

3,3′-Dicarbethoxydiamino-4,4′-dihydroxyarsenobenzene,

$$(C_2H_5OOC.HN)(HO)C_6H_3As = AsC_6H_3(OH)(NH.COOC_2H_5).$$

A pale yellow powder soluble in alcohol, acetone, alkali hydroxides or carbonates, insoluble in ether, benzene or dilute acids; prepared by reducing the corresponding arsonic acid with hydrosulfite. When warmed with hydrochloric acid it decomposes, yielding 3,3′-diamino-4,4′-dihydroxyarsenobenzene.[638]

4,4′-Dicarbethoxydiamino-2,2′-dihydroxyarsenobenzene results upon treating a methyl alcoholic solution of the corresponding arsonic acid with hypophosphorous acid containing a slight amount of potassium iodide. It separates as a pale yellow precipitate soluble in caustic soda.[639]

3,3′-Dicarbamido-4,4′-dihydroxyarsenobenzene,

$$(H_2NCONH)(HO)C_6H_3As = AsC_6H_3(OH)(NHCONH_2).$$

A pale yellow powder decomposing above 200° without melting, readily soluble in acetone, alcohol or sodium carbonate, and insoluble in water, ether or dilute mineral acids. It is prepared from the arsonic acid by reduction with sodium hydrosulfite.[638]

3,3′-N-Di(methylamino)-4,4′-dihydroxyarsenobenzene,

$$(H_3C.HN)(HO)C_6H_3As = AsC_6H_3(OH)(NH.CH_3),$$

is derived from the corresponding arsonic acid like the preceding compound. Its dihydrochloride is a grayish-white or yellow microcrystalline powder which with a dilute hydrochloric acid solution of 4-dimethylaminobenzaldehyde yields a brownish-orange liquid, but, unlike arsphenamine, no subsequent precipitate. The sparingly soluble sulfate is

formed by adding dilute sulfuric acid to an aqueous solution of the dihydrochloride.[640]

3,3′-Di(N-methylacetylamino)-4,4′-dihydroxyarsenobenzene,

$$\left(\begin{array}{l}CH_3\diagdown \\ \qquad\quad N \\ CH_3OC\diagup\end{array}\right)(HO)C_6H_3As = AsC_6H_3(OH)\left(\begin{array}{l}\quad\diagup CH_3 \\ N \\ \quad\diagdown COCH_3\end{array}\right),$$

is prepared by adding acetic anhydride to an alkaline solution of the preceding compound. The precipitate is readily soluble in aqueous alkalis, but insoluble in dilute hydrochloric acid.[641]

3,3′-Tetramethyldiamino-4,4′-dihydroxyarsenobenzene,

$$[(H_3C)_2N](HO)C_6H_3As = AsC_6H_3(OH)[N(CH_3)_2],$$

is made like the corresponding dimethyl compound. Its dihydrochloride is a yellowish-white powder easily soluble in water or methyl alcohol and slowly yields a precipitate with sulfuric acid in aqueous solution.[641]

3,3′-Hexamethyldiammonium-4,4′-dihydroxyarsenobenzene,

$$\left[\begin{array}{l}(H_3C)_3\diagdown\!\!\!\diagdown\!\!\!\diagdown \\ \qquad\qquad N \\ \quad HO\diagup\end{array}\right](HO)C_6H_3As = AsC_6H_3(OH)\left[\begin{array}{l}\quad\diagup\!\!\!\diagup\!\!\!\diagup(CH_3)_3 \\ N \\ \quad\diagdown OH\end{array}\right],$$

is a light yellow powder easily soluble in aqueous caustic soda or dilute hydrochloric acid, but insoluble in water. It is prepared by reducing 3-trimethylammonium-4-hydroxyphenylarsonic acid with sodium hydrosulfite at ordinary temperature.[642]

3,3′-Diamino-4,4′-dimethoxyarsenobenzene,

$$(H_2N)(CH_3O)C_6H_3As = AsC_6H_3(OCH_3)(NH_2),$$

may be prepared either from 3-acetylamino-4-methoxyphenylarsonic acid by hydrolyzing with hydrochloric acid, rendering alkaline, and reducing with sodium hydrosulfite, or from 3-nitro-4-methoxyphenylarsonic acid by reducing with the same reagent. The dihydrochloride, a yellow, water-soluble powder containing $2H_2O$, results upon dissolving the base in absolute methyl alcoholic hydrochloric acid and precipitating with ether. With an excess of caustic soda, the salt yields a yellow insoluble precipitate, which dissolves to a colorless solution upon oxidation with iodine. Sodium sulfate, added to an aqueous solution of the dihydrochloride, precipitates the sulfate; sodium acetate, the free base;

while 4-dimethylaminobenzaldehyde yields an orange-colored precipitate. Upon diazotizing with sodium nitrite in dilute hydrochloric acid solution, there is produced a yellow solution, which couples with α-naphthylamine hydrochloride in alcoholic solution to a deep purple coloration. Ferric chloride oxidizes the aqueous solution of the dihydrochloride more slowly than in the case of arsphenamine.[643]

3,3'-Diamino-4,4'-dimethoxy-5,5'-dimethylarsenobenzene,

$$(H_2N)(CH_3O)(H_3C)C_6H_2As = AsC_6H_2(CH_3)(OCH_3)(NH_2).$$

Prepared by reducing the corresponding nitro arsonic acid with sodium hydrosulfite.[644] The dihydrochloride is a faintly yellow powder readily soluble in water or methyl alcohol, less so in ethyl alcohol, and insoluble in ether or acetone. It contains two molecules of water and decomposes at 186°. Concentrated hydrochloric acid reprecipitates the dihydrochloride from aqueous solution, but dilute sulfuric acid produces no precipitate.

3,3'-Diamino-4,4'-dihydroxy-6,6'-dimethoxyarsenobenzene,

$$(H_2N)(CH_3O)(HO)C_6H_2As = AsC_6H_2(OH)(OCH_3)(NH_2).$$

The corresponding arsonic acid is reduced with hypophosphorous acid containing a slight amount of potassium iodide, and the arseno compound precipitated either as the hypophosphite by gradually introducing the resulting yellow solution into acetone with continuous stirring in an atmosphere of carbon dioxide, or as the dihydrochloride by employing concentrated hydrochloric acid. Upon warming an aqueous solution of the latter salt, the arsenic is split off yielding 4-amino-3-hydroxy-1-methyl ether.[645]

3,3'-Diamino-4,6,4',6'-tetramethoxyarsenobenzene,

$$(H_2N)(CH_3O)C_6H_2As = AsC_6H_2(OCH_3)(NH_2).$$

Prepared from the corresponding nitro arsonic acid by reduction with hydrosulfite. Its dihydrochloride separates upon dissolving in methyl alcoholic hydrochloric acid and precipitating with ether.[646]

3,3'-Tetramethyldiamino-4,4'-dimethoxyarsenobenzene,

$$[(H_3C)_2N](CH_3O)C_6H_3As = AsC_6H_3(OCH_3)[N(CH_3)_2],$$

results upon adding acetic anhydride to an alkaline solution of the corresponding tetramethyldiaminodihydroxyarseno compound. It is readily soluble in dilute hydrochloric acid, but dissolves very slowly in aqueous caustic soda.[641]

5,5′-Dichloro-3,3′-diamino-4,4′-dihydroxyarsenobenzene dihydrochloride,

$$\left(\begin{array}{ccccc} HCl.H_2N & & & & NH_2.HCl \\ & \diagdown & & \diagup & \\ HO - & C_6H_2As & = & AsC_6H_2 & - OH \\ & \diagup & & \diagdown & \\ Cl & & & & Cl \end{array}\right).2CH_3OH,$$

is a greenish-yellow powder prepared by reducing the corresponding nitro arsonic acid with sodium hydrosulfite at 55°, dissolving the resulting arseno compound in methyl alcoholic hydrochloric acid, and precipitating with absolute ether. With an excess of aqueous silver nitrate in diluted methyl alcohol, it forms a yellow disilver chloride addition product, $(AgCl.H_2N)(HO)ClC_6H_2As = AsC_6H_2Cl(OH)(NH_2.AgCl)$; with cupric chloride it yields a yellowish-brown addition product,

$$[(H_2N)(O\frac{Cu}{2})ClC_6H_2As =]_2.CuCl_2,$$

containing four molecules of water.[647]

5,5′-Dichloro-4,4′-diamino-3,3′-dihydroxyarsenobenzene. — 3,5-Dichloro-p-arsanilic acid is diazotized with potassium pyrosulfite and concentrated nitric acid, treated with sodium acetate, and stirred until coupling with R-salt no longer takes place, indicating a complete replacement of one of the chlorine atoms by a hydroxyl group. The product is now coupled with alkaline β-naphthol, the resulting azo dye collected, redissolved in hot water, and the dye acid precipitated by acidifying with mineral acid. The precipitate is dissolved in water containing sodium hydroxide and acetate, and warmed with sodium hydrosulfite at 40-45° until decolorization occurs. After cooling, the precipitated 1-amino-β-naphthol is filtered off, and the filtrate reduced to the arseno compound by warming with more hydrosulfite at 60°. The product is a yellow powder readily soluble in aqueous caustic soda or dilute hydrochloric acid. The dihydrochloride is precipitated by concentrated hydrochloric acid.[648]

5,5′-Diiodo-3,3′-diamino-4,4′-dihydroxyarsenobenzene,

$$\begin{array}{ccccc} H_2N & & & & NH_2 \\ & \diagdown & & \diagup & \\ HO - & C_6H_2As & = & AsC_6H_2 & - OH \\ & \diagup & & \diagdown & \\ I & & & & I \end{array}.$$

The therapeutic properties of this compound have been studied by Ehrlich.[649]

5,5′-Disulfo-3,3′-diamino-4,4′-dihydroxyarsenobenzene,

$$\begin{array}{ccc} H_2N & & NH_2 \\ \diagdown & & \diagup \\ HO - C_6H_2As & = & AsC_6H_2 - OH \\ \diagup & & \diagdown \\ HO_3S & & SO_3H \end{array} ,$$

may be obtained from the corresponding arsonic acid by suspending in acetic acid containing a crystal of potassium iodide, and warming with hypophosphorous acid at 55°,[650] or from the corresponding arsenious acid by reducing either with sodium hydrosulfite at 50°, or with hypophosphorous acid in acetic acid medium at 100°.[651] According to King, this compound is one of the sulfur derivatives formed in the preparation of arsphenamine from 3-nitro-4-hydroxyphenylarsonic acid and sodium hydrosulfite. He succeeded in obtaining it in small amounts by reducing an alkaline solution of the above nitro compound with sodium hydrosulfite at —2° and allowing to stand in the cold over night. After filtering off the crystals of 3-amino-4-hydroxyphenylarsonic acid, the filtrate is rendered slightly acid with concentrated hydrochloric acid and maintained at 0° or below for one week, when a mixture of sodium sulfate, 5-sulfo-3-amino-4-hydroxyphenylarsenious acid and 5,5′-disulfo-3,3′-diamino-4,4′-dihydroxyarsenobenzene separates out. The first is removed with water at 40°, the remaining mixture of the two arsenicals suspended in water, dissolved with the aid of ammonia, and the calcium salt of the arseno compound precipitated by the addition of calcium chloride solution. The free arseno compound is then obtained from the salt by treating with hydrochloric acid.[544]

The dried product is a fawn-colored powder insoluble in water or acids, and may be diazotized to a deep yellow solution. Although it dissolves in dilute ammonia, sodium hydroxide or carbonate solution, it is reprecipitated by an excess of the concentrated reagent. The product also dissolves in aqueous sodium bicarbonate or acetate. The ammoniacal solution yields a copious gelatinous precipitate with calcium or barium chloride, magnesia mixture, lanthanium or thorium nitrate, and only a very slight precipitate with lithium chloride.

2,2′-Dicarboxyarsenobenzene (o-Arsenobenzoic acid),

$$HOOC.C_6H_4As = AsC_6H_4.COOH,$$

prepared from 2-carboxyphenyldiiodoarsine by boiling with phosphorous acid in alkaline solution, is a yellow powder easily soluble in alkali hydroxides or carbonates, and practically insoluble in alcohol, benzene, ether, chloroform or hot water. Heated over a direct flame, it first melts, and then partially decomposes with the separation of free arsenic.[652]

4,4′-Dicarboxyarsenobenzene (p-Arsenobenzoic acid), is a yellow powder decomposing on heating without melting, soluble in alkalis, and

insoluble in water or the usual organic solvents. It is obtained by heating an aqueous solution of p-benzarsenious acid with phosphorous acid. The sodium salt is a yellowish-brown amorphous powder easily soluble in water but difficulty in dilute caustic soda.[653]

p-Arsenomyricylbenzoate,

$$H_{61}C_{30}.O.OC.C_6H_4As = AsC_6H_4.CO.O.C_{30}H_{61},$$

from the arsineoxide and phosphorous acid in boiling acetone solution, is a pale yellow powder soluble in alcohol, ether or benzene.[106]

p-Arsenocholesterylbenzoate,

$$H_{44}C_{27}.O.OC.C_6H_4As = AsC_6H_4.CO.O.C_{27}H_{44},$$

a yellow powder soluble in benzene or chloroform, is prepared like the previous compound.[106]

p-Arsenoquininebenzoate,

$$O_2N_2H_{23}C_{20}.O.OC.C_6H_4As = AsC_6H_4.CO.O.C_{20}H_{23}N_2O_2,$$

is a bright yellow powder soluble in acids, difficultly so in organic solvents, and insoluble in water, alkali hydroxides or carbonates. It results upon warming a sodium carbonate solution of the quinine ester of 4-carboxyphenylarsonic acid with sodium hydrosulfite at 50-60°.[504]

p-Arsenostovaine,

$$\begin{array}{rcl} C_2H_5 \diagdown & & \diagup C_2H_5 \\ CH_3 - & COOCC_6H_4As = AsC_6H_4COOC & - CH_3 \\ (CH_3)_2NCH_2 \diagup & & \diagdown CH_2N(CH_3)_2, \end{array}$$

obtained from the corresponding arsineoxide and sodium hydrosulfite, is a golden-yellow powder soluble in acids and insoluble in water or alkalis. When freshly prepared, it dissolves in organic solvents.[546]

p-Arsenohippuric acid,

$$HOOCH_2CHNOC.C_6H_4As = AsC_6H_4.CONHCH_2COOH,$$

from the corresponding arsonic acid and sodium hydrosulfite, is a yellow powder forming unstable solutions with alkali carbonates or phosphates, but stable solutions with caustic alkalis in the absence of air.[547]

The following six arseno compounds, prepared by reduction of their respective arsineoxides, are yellow amorphous powders practically insoluble in water, and difficultly soluble in alcohol: *p-arsenobenzoylalanine*

$$\begin{array}{l}CH_3\\HOOC\end{array}\!\!>CH.HNOC.C_6H_4As=AsC_6H_4.CONH.CH<\begin{array}{l}CH_3\\COOH\end{array}$$

p-arsenobenzoylphenylalanine,

$$\begin{array}{l}C_6H_5.CH_2\\HOOC\end{array}\!\!>CH.HNOC.C_6H_4As=AsC_6H_4.CONH.CH<\begin{array}{l}CH_2.C_6H_5\\COOH\end{array}$$

p-arsenobenzoyltyrosine,

$$\begin{array}{l}AsC_6H_4CONHCH<\begin{array}{l}CH_2C_6H_4(OH)\\COOH\end{array}\\ \| \\ AsC_6H_4CONHCH<\begin{array}{l}CH_2C_6H_4(OH)\\COOH\end{array}\end{array}$$

p-arsenobenzoylleucine,

$$\begin{array}{l}AsC_6H_4CONHCH<\begin{array}{l}CH_2CH(CH_3)_2\\COOH\end{array}\\ \| \\ AsC_6H_4CONHCH<\begin{array}{l}CH_2CH(CH_3)_2\\COOH\end{array}\end{array}$$

p-arsenobenzoylaspartic acid,

$$\begin{array}{l}HOOCCH_2\\HOOC\end{array}\!\!>CH.HNOC.C_6H_4As=AsC_6H_4.CONH.CH<\begin{array}{l}CH_2COOH\\COOH\end{array}$$

and *p-arsenobenzoylglutamic acid,*

$$\begin{array}{l}AsC_6H_4CONHCH<\begin{array}{l}CH_2CH_2COOH\\COOH\end{array}\\ \| \\ AsC_6H_4CONHCH<\begin{array}{l}CH_2CH_2COOH\\COOH\end{array}\end{array}$$

4,4'-Diacetyldiamino-3,3'-dicarboxyarsenobenzene, [*Arsenoacetylanthranilic acid*],

$$(CH_3CO.HN)(HOOC)C_6H_3As=AsC_6H_3(COOH)(NHCOCH_3).$$

A pale yellow powder soluble in alkalis, also in alcohol when freshly precipitated, and insoluble in water. It is made from the corresponding arsonic acid by reduction with sodium hydrosulfite at 30-40°.[520]

4,4′-Dihydroxy-2,2′-dicarboxyarsenobenzene,

$$(HOOC)(HO)C_6H_3As = AsC_6H_3(OH)(COOH).$$

4-Amino-2-carboxyphenylarsonic acid is diazotized at 5°, the diazonium salt warmed until all nitrogen has been evolved, and the resulting solution of 4-hydroxy-2-carboxyphenylarsonic acid reduced with hypophosphorous acid containing a small amount of potassium iodide.[654]

5,5′-Dinitro-4,4′-dihydroxy-2,2′-dicarboxyarsenobenzene,

$$(O_2N)(HO)(HOOC)C_6H_2As = AsC_6H_2(COOH)(OH)(NO_2).$$

Prepared by boiling the corresponding arsonic acid with hypophosphorous and glacial acetic acids.[655]

5,5′-Diamino-4,4′-dihydroxy-2,2′-dicarboxyarsenobenzene,

$$(H_2N)(HO)(HOOC)C_6H_2As = AsC_6H_2(COOH)(OH)(NH_2),$$

is obtained from the preceding compound by suspending in dilute acetic acid and adding a slight amount of potassium iodide. It is easily soluble in sodium hydroxide, carbonate, bicarbonate or acetate solution, sparingly in dilute or concentrated hydrochloric acid, and forms a red condensation product with 4-dimethylaminobenzaldehyde. Like other primary amines it can be readily diazotized. Heating a dilute sodium acetate solution of the arseno compound in a sealed tube for ten hours on a water-bath, converts it into 4-amino-3-hydroxybenzoic acid.[655]

5,5′-Diamino-4,4′-dihydroxy-3,3′-dicarboxyarsenobenzene is obtained by reducing the corresponding nitro arsonic acid.[656]

3-Amino-4-hydroxybenzenearsenomethane,

$$(H_2N)(HO)C_6H_3As = AsCH_3,$$

is prepared by reducing a mixture of 3-amino-4-hydroxyphenylarsineoxide and methylarsineoxide in dilute methyl alcoholic solution with sodium hydrosulfite, or by digesting a mixture of disodium methylarsonate and 3-amino-4-hydroxyphenylarsonic acid with alkaline hydrosulfite and magnesium chloride at 50°. The product is a yellow powder soluble in dilute hydrochloric acid or caustic soda.

Its yellow hydrochloride is obtained by reducing a methyl alcoholic hydrochloric acid solution of 3-amino-4-hydroxyphenylarsonic acid and methylarsineoxide at —20° to —10° with an acetone solution of stannous chloride and concentrated hydrochloric acid in the presence of a slight amount of hydriodic acid.[657]

3-Amino-4-hydroxyarsenobenzene, $(H_2N)(HO)C_6H_3As = AsC_6H_5$.— Obtained by reducing a mixture of 3-amino-4-hydroxyphenyl- and phenyl

arsineoxides,[538] or by condensing 3-amino-4-hydroxyphenylarsine in methyl alcoholic hydrochloric acid solution with phenylarsineoxide dissolved in benzene, and treating the resulting hydrochloride with the requisite amount of caustic soda.[523] The base is a pale yellow powder soluble in alcohol, acetone, dilute hydrochloric acid or caustic soda, and insoluble in water, benzene, chloroform or aqueous sodium carbonate. The hydrochloride is a yellow powder soluble in water, methyl or ethyl alcohol.

4-Amino-4′-hydroxyarsenobenzene, $H_2N.C_6H_4As = AsC_6H_4.OH$, is a yellow powder decomposing at 200°, soluble in hydrochloric acid or caustic soda, and insoluble in water or the usual organic solvents. It results upon mixing a methyl alcoholic solution of 4-hydroxyphenylarsineoxide with a dilute hydrochloric acid solution of 4-aminophenylarsine, allowing to stand for several hours, and finally precipitating with sodium acetate solution.[523]

3,4′-Diamino-4-hydroxyarsenobenzene dihydrochloride,

$$(HCl.H_2N)C_6H_4As = AsC_6H_3(OH)(NH_2.HCl).$$

A mixture of equimolar quantities of 3-amino-4-hydroxyphenylarsonic acid and either 4-aminophenyl arsonic acid or arsineoxide in methyl alcoholic hydrochloric acid is reduced with alcoholic stannous chloride-hydrochloric acid containing a slight amount of hydriodic acid. It separates as a yellow, microcrystalline precipitate soluble in water to a clear solution, which yields no precipitate with an excess of alkali indicating the absence of any 3,3′-diaminoarsenobenzene. Dilute sulfuric acid precipitates a pale yellow, insoluble sulfate.[538]

3-Amino-4-hydroxyarsenobenzene-4′-glycine,

$$(H_2N)(HO)C_6H_3As = AsC_6H_4(NH.CH_2COOH).$$

Prepared by mixing a methyl alcoholic solution of 4-dichloroarsinophenylglycine hydrochloride and 3-amino-4-hydroxyphenylarsineoxide with dilute caustic soda and reducing with sodium hydrosulfite,[538] or by condensing 3-amino-4-hydroxyphenylarsine with either 4-dichloroarsinophenylglycine or the corresponding arsineoxide.[523] The product is a brownish powder darkening at 120° and decomposing at 150° without melting. It is insoluble in water, alcohol or the usual organic solvents, but is easily soluble in aqueous sodium hydroxide, carbonate or bicarbonate, dilute hydrochloric, glacial acetic or concentrated sulfuric acid. When heated with tin and hydrochloric acid, it decomposes, yielding phenyl(-4-glycine)- and 3-amino-4-hydroxyphenyl arsines.

3′,5′-Dichloro-3-amino-4,4′-dihydroxyarsenobenzene,

$$(H_2N)(HO)C_6H_3As = AsC_6H_2Cl_2(OH),$$

results upon reducing an alkaline methyl alcoholic solution of 3,5 dichloro-4-hydroxyphenylarsineoxide and 3-amino-4-hydroxyphenyl arsineoxide with sodium hydrosulfite. The product is a bright yellow powder insoluble in water, soluble in ether, acetone, methyl or ethy alcohol, dilute hydrochloric acid, aqueous sodium hydroxide or carbonate and less so in sodium bicarbonate.[538]

3-Amino-4-hydroxy-3′,4′,5′-triaminoarsenobenzene trihydrochloride $(H_2N)(HO)C_6H_3As = AsC_6H_2(NH_2)_3$, 3HCl.—A mixture of 3,4,5,3′,4′ 5′-hexaaminoarsenobenzene hydrochloride and arsphenamine in aqueou solution is rapidly warmed to 80° and poured into concentrated hydro chloric acid, the above hydrochloride separating in yellow flakes which unlike hexaaminoarsenobenzene, are easily soluble in aqueous sodium hydroxide and in contrast with arsphenamine are also soluble in sodium bicarbonate.[598]

4-Methylamino-3,5,3′,4′,5′-pentaaminoarsenbenzene tetrahydrochloride, $(H_2N)_3C_6H_2As = AsC_6H_2(NH_2)_2(NH.CH_3)$, 4HCl.—Prepared like the preceding compound from 3,4,5,3′,4′,5′-hexaaminoarsenobenzene and 4,4′-bismethylamino-3,5,3′,5′-tetraaminoarsenobenzene hydrochlorides by precipitating with glacial acetic acid. The product is easily soluble in water, and forms a stable carbonate derivative with sodium bicarbonate.[598]

5-Sulfo-3,3′-diamino-4,4′-dihydroxyarsenobenzene hydrochloride,

$$(HCl.H_2N)(HO)C_6H_3As = AsC_6H_2(OH)(NH_2)(SO_3H),$$

is obtained by reducing a mixture of equimolar amounts of 5-sulfo-3-amino-4-hydroxyphenylarsonic acid and 3-amino-4-hydroxyphenylarsonic acid either with a mixture of hypophosphorous and acetic acids containing a small quantity of potassium iodide at 60°, or with sodium hydrosulfite at 50-55°, and treating the resulting base with aqueous hydrochloric acid. It is sparingly or slowly soluble in water, insoluble in aqueous sodium bicarbonate, and readily soluble in dilute caustic soda, but is reprecipitated by an excess of the latter. It is also soluble in dilute or concentrated ammonia, and slowly in aqueous sodium carbonate, from which it is not reprecipitated by an excess of the reagent. The ammoniacal solution yields gelatinous precipitates with calcium, barium or magnesium chlorides, and with an excess of lithium chloride.[658]

Polyarsenides.

Upon adding sodium hydrosulfite and magnesium chloride to a neutral solution of phenylarsonic acid and sodium arsenite, and allowing

to stand for 24 hours at ordinary temperature, a light yellow precipitate of the polyarsenide is formed. It contains about 54% of arsenic, is easily soluble in chloroform, sparingly so in the other organic solvents, and insoluble in water, mineral acids or alkalis.[659]

Upon passing arsine through an alcoholic solution of phenyldichloroarsine, there is obtained a yellow precipitate insoluble in water, alcohol or ether.[568]

4-Aminophenylarsineoxide yields a polyarsenide when mixed with one molecular proportion of arsenic trichloride in methyl alcohol, and reduced with a cold solution of stannous chloride and concentrated hydrochloric acid in the same solvent. The product separates as a brownish-yellow precipitate soluble in moist pyridine or hot dilute hydrochloric acid. The latter solution yields a precipitate with dilute sulfuric acid or an excess of caustic soda.[659]

A yellow precipitate soluble in pyridine or dilute hydrochloric acid is obtained by treating an alcoholic solution of 4-aminophenyldichloroarsine with arsine.[568]

When a mixture of equimolar amounts of 3-amino-4-hydroxyphenylarsonic acid and sodium arsenite is reduced with sodium hydrosulfite at 50-55°, an orange-yellow precipitate containing 48.9% of arsenic is obtained. It is difficultly soluble in ether, benzene, alcohol or concentrated hydrochloric acid, readily soluble in aqueous caustic soda or dilute hydrochloric acid, and forms a sparingly soluble sulfate. When oxidized with hydrogen peroxide in alkaline solution, it yields arsenic- and 3-amino-4-hydroxyphenylarsonic acids.[660] Its methyl alcoholic hydrochloric acid solution reacts with metallic salts, yielding coördination compounds which can be precipitated by ether. The product with cuprous chloride is a pale brown powder soluble in water or methyl alcohol, and forms a sparingly soluble sulfate. Its copper is not precipitated by caustic alkalis. The mercuric chloride addition product, an orange powder insoluble in water or methyl alcohol, is blackened by caustic soda due to decomposition. Its coördination compound with silver nitrate is a brown powder readily soluble in water or methyl alcohol, and does not give the ionic reactions of silver.[661] The cupric chloride compound is obtained as a hydrochloride by reducing a mixture of 3-amino-4-hydroxyphenylarsineoxide, arsenic trichloride and hydrated cupric chloride with a cold solution of stannous chloride in concentrated hydrochloric and glacial acetic acids. It forms a brown powder soluble in water, methyl alcohol or aqueous caustic soda.[589]

With two moles of sodium arsenite, the above arsonic acid yields a brownish-red polyarsenide containing 57% of arsenic. It is easily soluble in dilute sodium hydroxide, the solution remaining clear when acidified with hydrochloric acid, even though the original product dissolves with difficulty in hydrochloric acid alone. Sulfuric acid precipitates the sulfate from the above hydrochloric acid solution.[659]

Polyarsenides containing varying amounts of arsenic may be obtained from 3-amino-4-hydroxyphenylarsonic acid by first converting into the arsineoxide, mixing with varying amounts of sodium arsenite, and reducing with hypophosphorous acid.[662]

On passing arsine through either an alcoholic solution of 3-amino-4-hydroxyphenyldichloroarsine hydrochloride,[568] or a glacial acetic acid solution of the corresponding arsineoxide,[569] and subsequently precipitating with ether, there is obtained a yellowish-brown powder easily soluble in dilute hydrochloric acid or alkalis.

Arsenophosphides.

An alcoholic solution of phenylarsineoxide, when treated with phosphine, yields a yellow precipitate which is very difficultly soluble in water, alcohol, acids or alkalis.[569]

Similarly, 4-aminophenyldichloroarsine hydrochloride or the corresponding arsineoxide yields a bright yellow powder easily soluble in water, from which it is reprecipitated by alkalis.[568] It forms a black addition product with silver nitrate.[663]

From 3-nitro-4-aminophenyl dichloroarsine[568] or arsineoxide,[569] a yellow powder soluble in dilute hydrochloric acid separates.

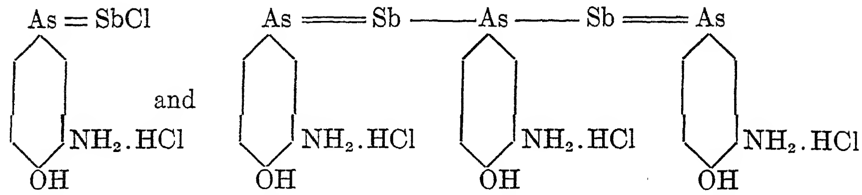
On passing phosphine through an alcoholic solution of 3-amino-4-hydroxyphenyldichloroarsine and precipitating with ether, a yellow powder is obtained which is easily soluble in water, dilute hydrochloric acid or alkalis.[848] Its addition product with cupric chloride, a red-brown powder soluble in alkalis or dilute hydrochloric acid, loses none of its copper when treated with either hydrogen sulfide or sodium hydrosulfite.[663]

Arsenoantimonides.

An alcoholic solution of 4-aminophenyldichloroarsine hydrochloride, when treated with stibine, yields a dark brown product soluble in dilute hydrochloric acid.[568]

3-Amino-4-hydroxyphenylarsineoxide, by treatment with stibine in glacial acetic acid solution and subsequent precipitation with ether, yields a brown powder soluble in dilute alkalis or hydrochloric acid.[569]

On mixing a methyl alcoholic hydrochloric acid solution of 3-amino-4-hydroxyphenylarsine with a one mole of antimony trichloride in methyl alcohol and precipitating with ether, a reddish-brown product is obtained which is soluble in water, caustic alkalis, dilute hydrochloric acid, methyl or ethyl alcohol, glycerine or glycol. With dilute sulfuric acid a difficultly soluble sulfate is produced.[664] The above product appears to be a mixture of



Its coördination compound with cupric chloride, prepared by mixing equimolar quantities of 3-amino-4-hydroxyphenylarsine, antimony trichloride and hydrated cupric chloride in methyl alcohol and precipitating with ether, is readily soluble in dilute hydrochloric acid or alkalis.[663]

A brown powder, difficultly soluble in water or methyl alcohol, is obtained by boiling a glacial acetic acid solution of antimonyl chloride and the methyl ester of anthranilylarsine, $(CH_3OOC)(H_2N)C_6H_3AsH_2$, in the absence of air.[430]

p-(Bromostibarseno)acetanilide, $(CH_3CO.HN)C_6H_4.As = SbBr$, is a red-brown powder soluble in water or dilute hydrochloric acid; prepared by mixing 4-acetylaminophenylarsine and antimony tribromide in methyl alcoholic hydrochloric acid, and precipitating with ether.[665]

Hydrochloride of *1-(acetoxystibarseno)-3-amino-4-hydroxybenzene,* $(HCl.H_2N)(HO)C_6H_3As = Sb.O.COCH_3$. — Prepared by boiling 3-amino-4-hydroxyphenylarsine in methyl alcoholic solution with a glacial acetic acid solution of tartar emetic, the product separating as a brownish-yellow precipitate easily soluble in water, aqueous alkalis or dilute hydrochloric acid. The latter solution yields a sparingly soluble sulfate with sulfuric acid, and a precipitate of a Schiff base with 4-dimethylaminobenzaldehyde.[430]

Upon reducing a mixture of 3-amino-4-hydroxyphenylarsonic acid and tartar emetic with sodium hydrosulfite at 50-55°, a reddish-brown powder is obtained, which is soluble in dilute hydrochloric acid or aqueous caustic soda.[666]

4-Hydroxyphenylarsenostibinobenzene, $HO.C_6H_4As = SbC_6H_5$, prepared by condensing phenylstibineoxide, $C_6H_5.SbO$, with 4-hydroxyphenylarsine,[430] is a brown powder soluble in aqueous alkalis.

4,4'-Dihydroxyarsenostibinobenzene, $HO.C_6H_4As = SbC_6H_4.OH$, is derived from a mixture of the sodium salts of 4-hydroxyphenylarsonic and 4-hydroxyphenylstibonic acids by reducing with sodium hydrosulfite until precipitation is complete. The product is a brownish-black powder insoluble in water, but readily soluble in aqueous caustic soda, pyridine, acetone, methyl or ethyl alcohol.[666]

3-Amino-4-hydroxyarsenostibinobenzene,

$$(H_2N)(HO)C_6H_3As = SbC_6H_5.$$

Prepared by reducing a mixture of 3-amino-4-hydroxyphenylarsineoxide and phenylstibonic acid with sodium hydrosulfite at ordinary temperature. It is a brownish-yellow powder readily soluble in aqueous caustic soda, moist pyridine or methyl alcoholic hydrochloric acid.[666]

The hydrochloride is obtained directly by mixing 3-amino-4-hydroxyphenylarsine and phenyldichlorostibine, $C_6H_5SbCl_2$, in methyl alcoholic hydrochloric acid and precipitating with ether. The product is a yellowish-brown amorphous powder easily soluble in water, aqueous alkali, dilute hydrochloric acid, methyl alcohol, glycerine or glycol. Sulfuric acid precipitates a difficultly soluble sulfate.[667] It forms a yellowish-brown coördination product with gold chloride and a brownish-green product with osmium chloride, both compounds being readily soluble in water, but insoluble in ether.[668]

3-Amino-4-hydroxyarseno-4′-acetylaminostibinobenzene hydrochloride, $(HCl.H_2N)(HO)C_6H_3As{=}SbC_6H_4(NH.COCH_3)$, separates as dark brown flakes soluble in water, methyl alcohol or caustic soda on mixing a glacial acetic acid solution of 4-acetylaminophenyldiiodostibine with a methyl alcoholic hydrochloric acid solution of 3-amino-4-hydroxyphenylarsine and precipitating with ether.[668]

3-Amino-4-hydroxyarseno-3′-amino-4′-chlorostibinobenzene,

$$(H_2N)(HO)C_6H_3As{=}SbC_6H_3Cl(NH_2),$$

is a stable compound.[669]

4′-Acetylaminophenylstibinoarseno-4-phenylglycine,

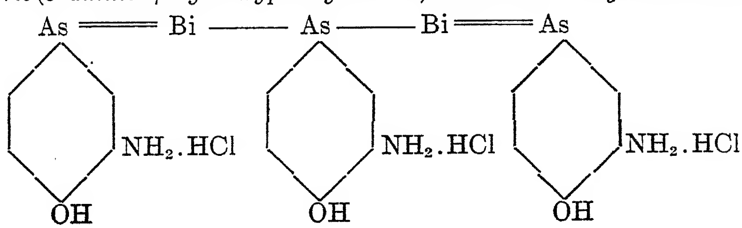
$$(HOOCCH_2.HN)C_6H_4As{=}SbC_6H_4(NHCOCH_3),$$

is obtained by reducing a mixture of phenylglycine-4-arsonic acid and 4-acetylaminophenylstibonic acid with sodium hydrosulfite in alkaline solution. It is a brownish-black powder insoluble in water, alcohol or acetone, but soluble in aqueous alkalis or moist pyridine.[666]

Arseno-Bismuth Compounds.

On mixing a methyl alcoholic hydrobromic acid solution of 4-acetylaminophenylarsine with bismuth tribromide in methyl alcohol solution and precipitating with ether, a black, sparingly soluble product is obtained which is gradually decomposed by acids or alkalis.[670]

Tris(3-amino-4-hydroxyphenylarseno)dibismuth trihydrochloride,



A mixture of 3-amino-4-hydroxyphenylarsine and bismuth trichloride in methyl alcoholic hydrochloric acid, when precipitated with ether, yields a black product readily soluble in methyl alcohol, glycerine or caustic alkalis, but very slowly in water. It is gradually decomposed by acids or alkalis, more readily by boiling the aqueous solution. Hydrogen peroxide in alkaline solution rapidly oxidizes it to 3-amino-4-hydroxyphenylarsonic acid and bismuth pentoxide.[671]

Arsphenamine.

(*"Salvarsan," "Arsenobenzol," "Diarsenol," "Kharsivan," "Arsenobillon," "606"* of Ehrlich's series.)

Although arseno compounds were first prepared by Michaelis in 1881, it remained for the genius of Ehrlich to build up step by step the remarkable substance which we know as Salvarsan, the dihydrochloride of 3,3′-diamino-4,4′-dihydroxyarsenobenzene. The clinical results following the administration of this drug during the past twelve years have definitely established the fact that it is the most remarkable synthetic chemical compound introduced into medicine. It is the premier medicament in the treatment of syphilis, yaws (frambœsia), relapsing fever and spirochetal infections in general. Mercury, which for four centuries had been employed in the treatment of syphilis, now occupies a position of secondary importance. That arsphenamine is superior to mercury is a virtually established fact. Its superiority is based not alone on the extremely rapid disappearance of syphilitic manifestations after its use, nor its success where mercury has failed, nor on its greater influence on the Wassermann reaction. Strongly supportive of the clinical evidence are laboratory studies on both animals and men.

Commercial samples of arsphenamine contain impurities, the exact nature of which is as yet undetermined. It has been found that samples obtained by reducing 3-nitro-4-hydroxyphenylarsonic acid with sodium hydrosulfite always contain small amounts of sulfur, the quantity depending upon the rate at which the solution of the nitrohydroxyphenylarsonic acid is introduced into the hydrosulfite solution, the initial temperatures of the two solutions, the rate of heating up to 55-60°, and the rate of stirring. Even in arsphenamine obtained by the hypophosphorous acid reduction of 3-amino-4-hydroxyphenylarsonic acid a very small amount of sulfur may be found, although in this case the quantity is smaller than that produced with any other method.[1518] According to Fargher[1519] the sulfur in arsphenamine exists partly in the form of a sulfamino group, —$NH.SO_3H$, the remainder being either attached to the arsenic or in

physical association with the arseno compound. King, however,[152] regards the main sulfur impurity as the monohydrochloride of 3,3′-di amino-4,4′-dihydroxy-5-sulfoarsenobenzene associated with varying pro portions of the sulfate of arsphenamine base.

Up to the present time it has not been definitely established whethe the formula of arsphenamine should be written with two molecules o water or one of methyl alcohol. On the one hand, Ehrlich[1521] an Kober[1522] claim that arsphenamine separates with $1CH_3OH$ when pre cipitated by the methyl alcohol-ether method, while, on the other hand Gaebel[1523] and Myers[1524] assume that it contains $2H_2O$. Fargher[151] found that arsphenamine precipitated as above contains no methy alcohol, free or combined, while Rieger[1525] obtained positive tests wit American, German and Canadian products. Kober further claims tha arsphenamine precipitated in aqueous hydrochloric acid contains eithe one or two molecules of water, depending upon the drying; that it i practically colorless when pure; and that the yellow tint of the othe commercial samples may be due to their sulfur contents. Raiziss an Falkov analyzed a number of commercial samples of arsphenamine fo carbon and hydrogen and found that some products contained on molecule of methyl alcohol, others contained two molecules of water o crystallization and the remainder contained both water of crystallizatio and methyl alcohol.[672]

In the course of his researches on salvarsan, Ehrlich investigated th interaction of this drug and various metallic salts, and as a result ther was synthesized a series of new coördination compounds in which eithe one or two molecular proportions of the metallic salt enters into intimat combination with the arseno compound. In these new complex com pounds the metal is held in a non-ionizable condition so that its ordinar ionic manifestations are practically entirely masked. The formation o these metallic complexes applies not only to all arseno compounds bu also to arsineoxides and arsines. The latter, however, in addition to thi strong residual affinity, have a tendency to simultaneously act as reduc ing agents. The ability of the arsineoxides to form coördination com pounds is less pronounced than that of the arseno compounds becaus the residual affinity of their arsenic is weaker, and is apparently greatl influenced by the substituents in the aromatic nucleus.

The coördination compounds of arsphenamine have been most thor oughly investigated on account of their therapeutic importance. The may be generally prepared by simply mixing the drugs with the metalli salt in methyl alcoholic solution and precipitating with ether. It is no necessary to first isolate arsphenamine, as the coördination compound are formed directly upon reducing mixtures of the metallic salts an the arsonic acid or arsineoxide. In a similar manner metalli

addition products have been obtained with the dialkali salts of arsphenamine.

There has been considerable discussion as to the constitution of these metallic coördination compounds, especially that of "silver arsphenamine." According to Karrer the metal attaches itself to the arsenic atoms, the resulting products corresponding to the formula

$$\left[\begin{array}{c} RAs\ldots Me \\ \| \\ RAs\ldots Me \end{array}\right]\begin{array}{c} X \\ \\ X \end{array},$$

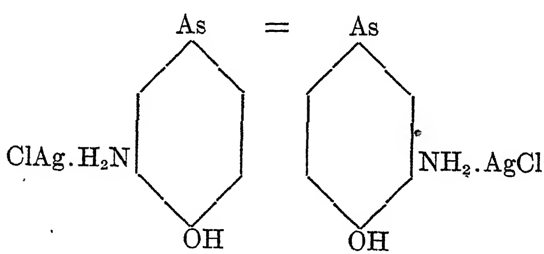
where Me represents the metallic and X the acid element or radicle. In accordance with this theory, the reaction between arsphenamine and two moles of silver nitrate proceeds in the manner indicated below:

$$\begin{array}{c} (HCl.H_2N)\,(HO)\,C_6H_3As \\ \| \\ (HCl.H_2N)\,(OH)\,C_6H_3As \end{array} \xrightarrow{2AgNO_3} \left[\begin{array}{c} (HCl.H_2N)HOC_6H_3As\ldots Ag \\ \| \\ (HCl.H_2N)HOC_6H_3As\ldots Ag \end{array}\right]\begin{array}{c} NO_3 \\ \\ NO_3 \end{array}$$

$$\longrightarrow \left[\begin{array}{c} (H_2N)\,(HO)\,C_6H_3As\ldots Ag \\ \| \\ (H_2N)\,(HO)\,C_6H_3As\ldots Ag \end{array}\right]\begin{array}{c} Cl \\ \\ Cl \end{array} + 2HNO_3.$$

On the other hand, Binz and his collaborators claim that arseno compounds containing no amino groups form no complexes with metallic salts, so that in silver arsphenamine the metal is attached to the nitrogen, the reaction proceeding according to the equation:

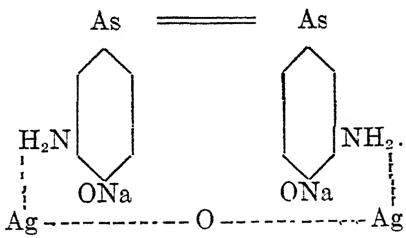
$$(HCl.H_2N)\,(HO)\,C_6H_3As = AsC_6H_3\,(OH)\,(NH_2.HCl) + 2AgNO_3 \longrightarrow$$

$\longrightarrow$  $+ 2HNO_3$

The silver compound dissolves in four molecular equivalents of aqueous sodium hydroxide, forming a disodium salt,

$$\begin{array}{c} (HOAg.H_2N)\,(NaO)\,C_6H_3As \\ \| \\ (HOAg.H_2N)\,(NaO)\,C_6H_3As \end{array},$$

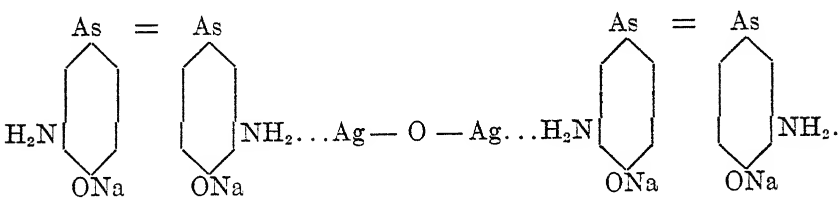
which immediately loses one molecule of water, yielding the anhydride



With one mole of silver nitrate arsphenamine forms a compound of the formula, $(H_2N)(HO)C_6H_3As = AsC_6H_3(OH)(NH_2.AgNO_3)$, which upon dissolving in three moles of caustic soda solution yields the silver hydroxide derivative,

$$(H_2N)(NaO)C_6H_3As = AsC_6H_3(ONa)(NH_2.AgOH),$$

the latter immediately losing $1H_2O$ and producing the anhydride



Bauer, after conducting a series of diffusion experiments and ultramicroscopic studies, concluded that silver arsphenamine is a chemically homogeneous substance in which the silver is held in complex combination. Raiziss, upon repeating these diffusion experiments not only with silver, but also with gold and platinum arsphenamines, found that although the arsenical completely passed through the membrane, the metal in each instance remained within the parchment bag. These results are in direct contrast to those of Bauer, and indicate that the metallic coördination compounds of arsphenamine are intimate mixtures of the drug and a colloidal form of the metal. The investigation of these compounds has been rendered difficult on account of the fact that they cannot be satisfactorily purified.

Very recently Binz and Ludwig claimed to have isolated two isomeric monosilver arsphenamine derivatives apparently corresponding to the formulæ, $(HCl.H_2N)(HO)C_6H_3As = AsC_6H_3(OH)(NH_2.AgCl)$ and

$$\begin{array}{l} (HCl.H_2N)(HO)C_6H_3As \\ \qquad\qquad\qquad\qquad\ \ \| \\ \qquad (H_2N)(HO)C_6H_3As.AgCl, \end{array}$$

which are converted into the corresponding silver hydroxide derivatives by means of alkalis. The exact formulæ, however, have not been definitely established.

Raiziss and Blatt prepared a new series of compounds consisting of

condensation products of arsphenamine and various aldehydes, in which one molecule of the aldehyde is attached to each amino group, and corresponding to the general formula,

$$[RCH(OH)HN](HO)C_6H_3As = AsC_6H_3(OH)[NH(HO)HCR].$$

They are prepared from disodium arsphenamine by mixing with slightly more than two moles of the aldehyde in methyl alcoholic solution in an atmosphere of nitrogen, either at ordinary or water-bath temperature, and finally neutralizing with hydrochloric acid. The compounds are solids varying in color from yellow to reddish-brown, cannot be recrystallized from the ordinary organic solvents, and are all, with the exception of the salicylaldehyde addition product, very sparingly soluble in alkali. The last property may be attributed to the fact that the solubility of phenolic compounds in dilute aqueous alkali is diminished by the introduction of groups into the phenol molecule: first, because of the resulting increased size of the molecule; and second, on account of the decreased acidity of the parent substance due to the nature and position of the group introduced.

Although wonderful results have been obtained in the treatment of syphilis by means of arsphenamine, the preparation of its solution for intravenous administration is not very convenient for the average physician. The drug must be dissolved in sterile water or physiological salt solution, and converted into its disodium salt by the careful addition of four molecular proportions of sodium hydroxide. Since this procedure complicates the practical application of the product, many attempts have been made to convert it into a stable compound having a similar therapeutic index $\frac{\text{(maximum tolerated dose)}}{\text{(minimum trypanocidal dose)}}$, and not only dissolving in water with a neutral reaction, but requiring no further preliminary treatment. This has been successfully attained in the elaboration of the drug "Neoarsphenamine," while of the numerous other, less efficient compounds the most prominent are "Sulfarsenol," "Galyl" and "Ludyl." Neoarsphenamine is a derivative of arsphenamine in which hydrogen of the amino groups is replaced by a sodium methylenesulfinate radical or radicals, the exact composition of the final product remaining as yet indefinite. In 1912, Ehrlich, in discussing this compound, merely described it as a condensation product of salvarsan with sodium formaldehydesulfoxylate, but furnished no analytical data as to its constitution. Later, Bertheim, in his monograph on organic arsenicals, ascribed to it the formula

$$(H_2N)(HO)C_6H_3As = AsC_6H_3(OH)[NH.CH(OH)SONa],$$

but Lehmann, after determining the arsenic content of several samples of the drug, concluded that the second amino group was not entirely

ree. Nevertheless, it had been generally assumed that neoarsphenamine vas the sodium salt of 3,3′-diamino-4,4′-dihydroxyarsenobenzene-N-nethylenesulfinic acid. In 1921, however, Raiziss and Falkov made a omplete study of the commercial product and found that it was a nixture of the N-mono- and N,N′-dimethylenesulfinates containing 'arying amounts of uncombined sodium formaldehydesulfoxylate, sodium ulfate and sodium chloride. It exhibits all the characteristic reactions f an arseno compound as well as the sodium salt of a substituted mino acid.

N-Substituted derivatives of arsphenamine have also been prepared y the interaction of its disodium salt with α-halogenated fatty acids. 'he products are generally yellow, amorphous substances soluble in lkalis, more or less so in dilute hydrochloric or sulfuric acid, and nsoluble in the usual organic solvents. These compounds have not as et been obtained in pure form, as no method has been developed for he removal of the admixed impurities or by-products which are always recipitated along with the main products.

3,3′-Diamino-4,4′-dihydroxyarsenobenzene (*Arsphenamine base*),

$$(H_2N)(HO)C_6H_3As = AsC_6H_3(OH)(NH_2).$$

'arious methods have been employed in the preparation of this most aluable therapeutic agent, but the most satisfactory procedure depends pon the direct reduction of 3-nitro-4-hydroxyphenylarsonic acid by neans of sodium hydrosulfite. Into a constantly stirred aqueous solution 13 l.) of crystallized magnesium chloride (513 g.) and sodium hydro-ulfite (2950 g. of 80 per cent) there is slowly introduced a cold solution f the above arsonic acid (197 g. = 0.75 mol.) in water (4.5 l.) con-aining sufficient caustic soda to form a disodium salt, and complete eduction effected by vigorous stirring at 55-60° for 1½ to 2 hours. 'he resulting yellow precipitate of the arsphenamine base is allowed to ettle, the supernatant liquid siphoned off, the residue transferred to uction funnels and washed with distilled water in an atmosphere of nert gas until the washings no longer exhibit an acid reaction. It is nen sucked as dry as possible, pressed on porous plates, and finally ried in vacuo over sulfuric acid. The crude 3,3′-diamino-4,4′-dihy-roxyarsenobenzene is contaminated with mineral ash and small quan-ities of arsenical compounds containing sulfur,[673] the greater part of 'hich is eliminated when the base is converted into its dihydrochloride. t has been claimed by Ehrlich,[674] that the magnesium chloride used in onjunction with the sodium hydrosulfite in the above reduction limits ne formation of arsenic-sulfur compounds.

According to Kober's modification,[675] the mixture of the arsonic acid nd hydrosulfite solutions is either permitted to stand at room tem-erature or is warmed on a water-bath at 40° until the suspension first

formed seems to agglutinate and about to settle, when it is rapidly filtered off, and the filtrate digested on a water-bath at 50-60° for 2-2½ hours.

Another method consists in boiling 3-nitro-4-hydroxyphenylarsonic acid (20 g.) with 25 per cent hypophosphorous acid (100 c.c.) and glacial acetic acid (70 c.c.), redissolving the precipitate of 3,3′-dinitro-4,4′-dihydroxyarsenobenzene by adding potassium iodide (12 g.) and finally precipitating the arsphenamine base by neutralization with soda.[676] This method may be modified by boiling the above arsonic acid (20 g.) with 100 c.c. of water, 60 g. of crystalline phosphorous acid, 80 c.c. of glacial acetic acid and 20 g. of potassium iodide.[676]

The same nitro compound may be reduced in successive stages by first forming 3-amino-4-hydroxyphenylarsonic acid, then 3-amino-4-hydroxyphenylarsineoxide, and finally arsphenamine base. Sodium amalgam (28.8 g. of 4 per cent Na) is added to a solution of the arsineoxide (4.98 g.) in water (30 c.c.) and 2N-acetic acid (32 c.c.), and the whole shaken from time to time at room temperature. When the amalgam has been completely utilized, a further addition of 25 c.c. of 2N-acetic acid and 28.8 g. of sodium amalgam is made, and the above treatment repeated until reduction is complete, as shown by testing a portion of the filtrate with sodium hydrosulfite. The precipitate of arsphenamine base is then washed and dried in the manner previously described.[677]

The above arsineoxide may also be reduced with hypophosphorous acid in precisely the same manner as the corresponding nitroarsonic acid.[676]

The 3-amino-4-hydroxyphenylarsonic acid yields the pure arseno compound directly upon warming with hypophosphorous acid and a small amount of potassium iodide at 60° for two hours in an atmosphere of carbon dioxide, and precipitating with a slight excess of 10 per cent sodium carbonate solution.[678]

Finally, arsphenamine base is obtained by condensing 3-amino-4-hydroxyphenylarsine with an equimolar amount of 3-amino-4-hydroxyphenylarsineoxide in ethyl alcoholic hydrochloric acid solution.[523]

The product is a pale yellow powder, soluble in dilute hydrochloric acid or aqueous alkali hydroxides, practically insoluble in aqueous sodium carbonate, and entirely so in water, sodium bicarbonate, dilute sulfuric acid or ether. It is reprecipitated from alkaline solution by neutralization with acids or by carbon dioxide. It is on account of the latter that an alkaline solution of arsphenamine becomes turbid on standing exposed to the air.

Dihydrochloride of 3,3′-diamino-4,4′-dihydroxyarsenobenzene ("Arsphenamine," "Salvarsan," "606" of Ehrlich's series, "Kharsivan," "Arsenobillon," "Diarsenol," "Arsenobenzol"),

$(HCl.H_2N)(HO)C_6H_3As = AsC_6H_3(OH)(NH_2.HCl)2H_2O$ or $1CH_3OH$.

Arsphenamine base (366 parts) is suspended in methyl alcohol (3000 parts) and dissolved by the addition of 25 per cent methyl alcoholic hydrochloric acid (292 parts). The solution is filtered, introduced into ten volumes of cold absolute ether with vigorous stirring and the resulting precipitate of the dihydrochloride filtered, washed with ether and thoroughly dried in vacuo over sulfuric acid. These operations should be carried out as much as possible under exclusion of air.[677, 679]

Another method consists in filtering off the precipitate of the base [obtained by reducing 3-nitro-4-hydroxyphenylarsonic acid with sodium hydrosulfite],[675] first washing with, then suspending in distilled water at 0°, and finally dissolving in the least amount of 2N-caustic soda at the same temperature. After filtering through an anaerobic filter, the solution is treated with 1:1 hydrochloric acid (150 c.c.) at 0°, the resulting liquid diluted to 1700 c.c. with distilled water, and slowly introduced with vigorous stirring into 1:1 hydrochloric acid (3250 c.c.) at 0°. The precipitate thus obtained, after settling for one hour, is filtered off and dried in vacuo over calcium chloride and solid caustic soda.[680]

The intermediate isolation of arsphenamine base may be avoided by the direct reduction of 3-amino-4-hydroxyphenylarsonic acid. The pure acid (23 g.) is mixed with water (736 c.c.), 50 per cent hypophosphorous acid (138 c.c.) and 3 per cent potassium iodide solution (11.5 c.c.), and the whole maintained at 55-60° for 1½ hours. After cooling the resulting deep-yellow solution to 10°, the dihydrochloride is precipitated by pouring into 1:1 hydrochloric acid (1640 c.c.) at 2° while stirring vigorously.[681] The corresponding arsineoxide may be employed instead of the arsonic acid in the above method, the reduction being carried out at room temperature instead of at 55-60°.[662]

Arsphenamine is a pale yellow powder, which has been obtained with a gray color by both Kober and Fargher. It is permanent when dry and preserved in vacuo or in an inert gas; is soluble in water, methyl alcohol, ethylene-glycol or glycerine, sparingly so in ethyl alcohol, and very sparingly in glacial acetic acid, acetone, ether or concentrated mineral acids. Its greenish-yellow aqueous solution reacts strongly acid to litmus, and is not visibly affected by concentrated phosphoric or dilute mineral acids, except dilute sulfuric acid. Arsphenamine base is completely reprecipitated from an aqueous solution of the salt by adding two moles of caustic alkali; a third mole redissolves the precipitate forming a monosodium phenolate, while a fourth mole produces a disodium salt, $(NaO)(H_2N)C_6H_3As=AsC_6H_3(NH_2)(ONa)$. It has recently been demonstrated that an aqueous solution of the latter is more efficacious in the treatment of syphilis than the monosodium salt. When a solution of the disodium salt is exposed to the air, it becomes more toxic due to a partial oxidation to 3-amino-4-hydroxyphenylarsineoxide,[42] which, according to Ehrlich,[682] is twenty times more toxic than arsphenamine, but according to Myers, is only six or seven times more toxic.[683]

The above base may also be obtained from the salt by treatment with sodium carbonate or acetate; it does not redissolve, however, in an excess of these reagents.

With phosphotungstic acid solution arsphenamine yields a dirty gray precipitate insoluble in excess of the reagent, but soluble to a deep blue solution in sodium carbonate or ammonia; with phosphomolybdic acid solution a similar color reaction is produced upon acidulating with hydrochloric acid after the addition of the alkali; while with Millon's reagent a yellow precipitate is obtained. 4-Dimethylaminobenzaldehyde added to a dilute hydrochloric acid solution of arsphenamine produces first an orange coloration and finally a precipitate of the same color. This reaction, distinct even in considerable dilutions, is rendered more so by the addition of mercuric chloride, and is suitable for detecting arsphenamine in animal tissues. When treated with sodium nitrite in dilute hydrochloric acid solution, the above arseno derivative forms a diazo compound having a greenish-yellow fluorescence, and producing a beautiful violet coloration with alcoholic α-naphthylamine, a light-brown color with alcoholic β-naphthylamine, and a deep red color with a freshly prepared alkaline solution of resorcinol.

Like other arseno compounds, arsphenamine is readily oxidizable—on exposure to the air, it oxidizes to the arsineoxide very slowly in aqueous solution, and even more slowly in the dry state. Although the solid can be preserved unchanged indefinitely in evacuated ampoules, its aqueous, methyl-alcoholic and especially its alkaline solutions undergo decomposition when kept for some time in evacuated and sealed containers. These solutions gradually darken, and finally deposit an intense reddish-brown precipitate possessing a complex structure and completely new properties, while the supernatant liquid becomes colorless. Since the earliest stages of this decomposition can scarcely be detected by chemical or physical means, biological and toxicological tests must be employed, the slightest alteration or decomposition of the drug causing an increase in toxicity. With iodine or alkaline hydrogen peroxide, arsphenamine is oxidized to 3-amino-4-hydroxyphenylarsonic acid; with mercuric chloride the corresponding arsineoxide is obtained.[495]

Arsphenamine sulfate is a yellowish-white precipitate very sparingly soluble in water, obtained by adding sulfuric acid or a soluble sulfate to an aqueous solution of the dihydrochloride.

Disodium salt of 3,3′-diamino-4,4′-dihydroxyarsenobenzene (Sodium arsphenamine), $(NaO)(H_2N)C_6H_3As = AsC_6H_3(NH_2)(ONa)$.—A 5 per cent solution of sodium methylate (190 g.) is added to a suspension of arsphenamine base (73 g.) in methyl alcohol (700 c.c.), and the resulting solution filtered into a mixture of absolute alcohol (1 l.) and ether (4 l.) accompanied by vigorous stirring. The precipitate formed is filtered off, washed with a mixture of equal parts of alcohol and ether, and dried in

vacuo. The entire procedure should be carried out in the complete absence of air.

The product is a greenish-yellow powder, readily soluble in water, but after long exposure to the air, its original solubility is diminished.[684] It is precipitated along with sodium formaldehyde sulfoxylate on adding the latter to a cold methyl alcoholic solution of the arseno compound, and pouring into an ice-cold mixture of alcohol and ether in the absence of air. The product is a pale-yellow powder readily soluble in water, but sparingly in alcohol.[685]

The dipotassium salt resembles the preceding compound, and is obtained by adding a methyl alcoholic solution (150 c.c.) of caustic potash (11.2 g.) to a suspension of arsphenamine base (36.6 g.) in methyl alcohol (120 c.c.), and precipitating with a mixture of alcohol (1 l.) and ether (3 l.) at 5°. Like the disodium compound, it must be prepared in the absence of air.[684]

An arsphenamine preparation, which is stable in evacuated ampoules, may be produced by dissolving arsphenamine (47.5 g.) in water (200 c.c.), converting into the disodium salt with 10N-sodium hydroxide (40 c.c. = 4 mols.), adding a solution of mannitol (17.2 g.) in water (100 c.c.), and precipitating with a mixture of absolute alcohol (4 l.) and ether (4 l.). The yellow powder obtained after drying is probably an intimate mixture of disodium arsphenamine and mannitol. It is readily soluble in water, very slightly so in alcohol or ether, and yields arsphenamine base with dilute hydrochloric acid.[686] Stable compounds are also obtained by mixing aqueous solutions of arsphenamine with the sodium salt of nucleinic acid, casein, protalbinic or lysalbinic acid. The resulting precipitate may be filtered off, washed and dried, or converted into the alkaline salt by dissolving the necessary amount of caustic alkali and either reprecipitating with alcohol-ether, or concentrating under diminished pressure. The free acid derivatives are yellow amorphous substances, while the colors of the sodium salts vary from green to light gray. The latter are easily soluble in water but insoluble in organic solvents.[687]

Co-ordination Compounds.

Arsphenamine—Silver Compounds.—Upon mixing equimolar quantities of arsphenamine and silver nitrate in methyl alcoholic solution and precipitating with ether, a brownish-yellow product is obtained which is very easily soluble in water, methyl alcohol or glycerine. The silver exists in a non-ionizable condition, and cannot be eliminated by the addition of reducing agents.[688] When slightly less than one molecular proportion of silver nitrate is added to an aqueous solution of arsphenamine, and the whole treated with concentrated aqueous sodium carbonate, a pale brown amorphous precipitate is obtained in which the

silver is attached to the amino group. It is insoluble in ammonia or soda solution, readily soluble in dilute hydrochloric acid or caustic soda, and is stable toward hypophosphorous acid. On adding aqueous caustic soda to the above mixture of the silver salt and arsphenamine, and passing carbon dioxide through the resulting solution, there is formed a dark brown precipitate whose silver is attached to the arsenic. It is soluble in ammonia, dilute hydrochloric acid, sodium hydroxide or carbonate, and yields metallic silver when warmed with hypophosphorous acid.[689] With two moles of silver nitrate arsphenamine yields a brown precipitate easily soluble in water, caustic soda or methyl alcohol, and yielding a brownish-yellow amorphous solid with sodium chloride.[688]

The disodium salt of the mono silver compound (*Silver Arsphenamine*) is prepared from arsphenamine either by dissolving in methyl alcohol, adding caustic soda solution (6 moles), mixing with methyl alcoholic silver nitrate solution (1 mole) and precipitating with absolute ether, or by mixing in aqueous medium with one mole of a silver salt, such as silver sulfate, and evaporating to dryness in vacuo.[690] It is a brownish-black powder, unstable in moist air, readily soluble in cold water, excess of dilute hydrochloric or nitric acid, concentrated sulfuric or nitric acid, but insoluble in saturated sodium bicarbonate solution, dilute sulfuric or concentrated hydrochloric acid. Upon the addition of dilute sodium hydroxide to an aqueous solution of "silver arsphenamine" no immediate change is noticeable, but upon exposure to air or oxygen, a silver mirror forms at the surface and gradually proceeds downward. With phosphotungstic acid a reddish precipitate is obtained; with phosphomolybdic acid a reddish-brown precipitate. In the presence of sodium carbonate, however, the latter two reagents produce a dirty green coloration. Picric acid added to an aqueous solution of silver arsphenamine produces a yellow precipitate, while ferric chloride yields first a reddish-colored solution, and finally a precipitate with an excess of the reagent.[691] According to Bauer,[692] silver arsphenamine is a chemically homogeneous substance, but the results of Raiziss and Gavron [693] indicate that it is an intimate mixture of arsphenamine and colloidal silver.

A mixture of *3,3'-diamino-4,4'-dihydroxyarsenobenzene disilver iodide*, $C_{12}H_{12}AS_2O_2N_2.2AgI$, and the *hydriodide of the corresponding monosilver iodide*, $C_{12}H_{12}As_2O_2N_2.AgI.HI$, is obtained by dissolving arsphenamine base (6.6 g.) in water (100 c.c.) and 2.9N-hydriodic acid (10 c.c.), and adding a solution of silver nitrate (3 g.) in water (75 c.c.). The resulting orange-colored precipitate, which turns brick red upon drying, forms a soluble sodium salt.[694]

A *monosilver bromide-arsphenamine* is obtained by adding a potassium cyanide solution of silver bromide (1 mole) drop by drop to a solution of arsphenamine (1 mole) until a permanent precipitate is formed, and, after redissolving with hydrochloric acid, the coördination product is precipitated as a sulfate by the addition of sulfuric acid.

The product is an orange-yellow to dark brown powder soluble in water rendered slightly alkaline by soda. The corresponding *chloro* and *iodo* derivatives may be similarly prepared.[96]

3,3'-Diamino-4,4'-dihydroxyarsenobenzene-silver bromide-antimonyl sulfate ("Luargol"), $(C_{12}H_{12}O_2N_2As_2)_2.AgBr.SbO(H_2SO_4)_2$, is prepared from the preceding compound by treating with antimony trichloride and precipitating with sulfuric acid.[97]

Arsphenamine—Gold Compounds.—To an aqueous solution of arsphenamine (5 c.c. of a 5 per cent solution), an equimolar amount of aqueous auric chloride or sodium aurate (2 c.c. of a 10 per cent solution) is added, and the coördination compound isolated either by concentrating in vacuo or by precipitating with alcohol-ether or alcohol-acetone.[695] The same product may be obtained by dissolving 3-amino-4-hydroxyphenylarsineoxide in a calculated quantity of dilute hydrochloric acid, adding an aqueous solution of 2.25 g. of auric chloride, and reducing with sodium hydrosulfite.[518] The brownish-yellow product is readily soluble in water, yields no precipitate of auric hydroxide with alkali, and loses none of its gold when treated with formaldehyde or sodium hydrosulfite in alkaline solution.

A compound containing two moles of auric chloride may be obtained by mixing methyl alcoholic solutions of arsphenamine (1.5 g.) and auric chloride (2 g.) and precipitating with ether. The product is a brownish-yellow powder soluble in water, caustic soda solution or alcohol.[696]

Silver and Gold Arsphenamine.—To a methyl alcoholic solution of arsphenamine (1.5 g.) there are added successively similar solutions of silver nitrate (0.55 g. = 1 mole) and auric chloride (1 g. = 1 mole), and precipitation effected by means of ether. The resulting compound exists as a brownish-red powder easily soluble in water, glycerine or other hydroxylic solvents, and contains one molecular proportion of arsphenamine, silver nitrate and auric chloride.[697]

Arsphenamine—Platinum Compound.—A brown powder, soluble in water, caustic soda or alcohols, is obtained by combining equimolecular proportions of the constituents either in methyl alcoholic [696] or in aqueous solution [695] and isolating like the corresponding gold compound. Its disodium salt is similarly prepared in alkaline solution.[695]

A coördination compound of arsphenamine and *palladium* prepared like the platinum derivative, is a brownish-black powder easily soluble in water or aqueous caustic soda.[698]

Arsphenamine—Copper Compounds.—A coördination product with one molecule of cupric chloride is obtained by dissolving arsphenamine

(100 g.) in methyl alcohol (1600 c.c.), adding successively saturated methyl alcoholic hydrochloric acid (16 c.c.), and a solution of crystalline cupric chloride (35.8 g. of $CuCl_2.2H_2O = 1$ mole) in methyl alcohol (400 c.c.) with stirring, and precipitating the coördination compound. The entire procedure should be carried out in an atmosphere of nitrogen or carbon dioxide.[699] The product may be similarly prepared in aqueous medium;[700] as well as by reducing either a hydrochloric acid solution of 3-amino-4-hydroxyphenylarsineoxide (2 moles) and crystalline cupric chloride (1 mole) with stannous chloride,[701] or a mixture of 3-amino-4-hydroxyphenylarsonic acid (2 moles) and cupric chloride (1 mole) with sodium hydrosulfite at 50°.[702] The product is an orange-yellow powder easily soluble in water, glycerine or ethylene glycol, and does not yield cupric hydroxide with aqueous alkalis in the cold, cupric oxide, however, separating upon warming.

The corresponding disodium salt is prepared either from the above coördination compound (40 g.) by dissolving in 2N-caustic soda (240 c.c.) and precipitating with alcohol (4 liters), or from a mixture of aqueous arsphenamine (5 g. in 40 c.c.) and aqueous cupric chloride (1.8 g. of $CuCl_2.2H_2O = 1$ mole in 15 c.c.) by rendering alkaline with 10N-caustic soda (8 c.c.) and precipitating with alcohol (900 c.c.). All operations in these two methods should be performed in an atmosphere of nitrogen.[703]

A di-cupric chloride derivative is similarly prepared from arsphenamine and 2 moles of the salt in methyl alcoholic solution.[699]

A mono cuprous derivative results upon mixing a methyl alcoholic solution of arsphenamine (3 g. in 20 c.c.) with a methyl alcoholic hydrochloric acid solution of cuprous chloride (1.24 g. = 1 mole) and precipitating with ether. It separates as a brick-red powder easily soluble in water.[697]

Arsphenamine — Mercuric Compound. — On dissolving equimolar quantities of arsphenamine and mercuric chloride in methyl alcohol containing a slight amount of hydrochloric acid and precipitating with ether, an orange colored powder is deposited. It is easily soluble in methyl alcohol, glycerine or acidified potassium iodide solution, insoluble in sodium chloride or potassium iodide solution, and is decomposed by water or aqueous caustic soda with separation of metallic mercury. If mercuric iodide is employed instead of the chloride, there is obtained a yellowish-red, water soluble product which is more stable than the mercuric chloride compound.[688]

Mercury and Antimony Arsphenamine.—When a methyl alcoholic solution of arsphenamine (10 g. in 100 c.c.) is mixed with similar solutions of antimony trichloride (4 g. in 4 c.c.) and mercuric iodide (1 g. in 90 c.c.) a cherry red solution is obtained from which ether precipitates

a yellowish-red powder easily soluble in water or a slight excess of aqueous caustic soda. Its methyl alcoholic alkali solution yields with ether a precipitate of a sodium compound containing arsphenamine base, mercuric iodide and an antimonyl radical.[704]

Condensation Products of Arsphenamine and Various Aldehydes.

3,3'-Bis[(hydroxymethyl)amino]-4,4'-dihydroxyarsenobenzene dihydrochloride,

$$[HCl.CH_2(OH)HN](HO)C_6H_3As = AsC_6H_3(OH)[NH(HO)CH_2.HCl],$$

is prepared by warming a methyl alcoholic solution of arsphenamine, formaldehyde (2 moles) and N-hydrochloric acid (5 moles) for two hours in an atmosphere of nitrogen, and finally precipitating with an excess of hydrochloric acid. It is a yellowish-brown powder decomposing at 190° without melting, soluble in methyl alcohol or hot water, sparingly in cold water or aqueous caustic soda, and insoluble in ether.[705]

3,3'-Bis(α-hydroxy-m-nitrobenzylamino)-4,4'-dihydroxyarsenobenzene,

$$\begin{array}{l} AsC_6H_3(OH)[NH(OH)HCC_6H_4.NO_2] \\ \| \\ AsC_6H_3(OH)[NH(OH)HCC_6H_4.NO_2] \end{array}$$

derived from disodium arsphenamine and 3-nitrobenzaldehyde (2 moles) by refluxing in methyl alcoholic medium for two hours in a current of nitrogen, is a yellow powder decomposing at 247-50° without melting, insoluble in water, dilute hydrochloric acid, methyl or ethyl alcohol, ether or benzene, and sparingly soluble in acetone, ethyl acetate or dilute caustic soda solution, gradually decomposing in the latter.[705]

3,3'-Bis(o,α-dihydroxybenzylamino)-4,4'-dihydroxyarsenobenzene,

$$\begin{array}{l} AsC_6H_3(OH)[NH(OH)HCC_6H_4.OH] \\ \| \\ AsC_6H_3(OH)[NH(OH)HCC_6H_4.OH] \end{array}$$

is a yellowish-brown powder, m. p. 182°, soluble in methyl alcohol or sodium hydroxide, sparingly so in glacial acetic acid, and insoluble in dilute mineral acids or organic solvents. It is prepared like the preceding compound by employing salicylaldehyde at ordinary temperature, and is completely precipitated upon acidifying the reaction mixture with hydrochloric acid. The corresponding dihydrochloride is obtained by the interaction of arsphenamine and salicylaldehyde (2 moles) in methyl alcoholic-hydrochloric acid solution and subsequently precipitating with ether. It is an orange-yellow powder soluble in dilute aqueous caustic

soda, sparingly so in hot acetone, and insoluble in acids or the usual organic solvents.[706]

3,3′-Bis(α-hydroxy-p-methoxybenzylamino)-4,4′-dihydroxyarsenobenzene,

$$\begin{array}{l} AsC_6H_3(OH)[NH(OH)HCC_6H_4(OCH_3)] \\ \| \\ AsC_6H_3(OH)[NH(OH)HCC_6H_4(OCH_3)] \end{array}$$

from disodium arsphenamine and p-anisaldehyde in the absence of air, is a yellow powder gradually decomposing on heating, sparingly soluble in dilute caustic soda solution, acetone or ethyl acetate, and insoluble in water, dilute hydrochloric acid, ether, methyl or ethyl alcohol.[706]

3,3′-Bis(p,α-dihydroxy-m-methoxybenzylamino)-4,4′-dihydroxyarsenobenzene,

$$\begin{array}{l} AsC_6H_3(OH)[NH(OH)HCC_6H_3(OH)(OCH_3)] \\ \| \\ AsC_6H_3(OH)[NH(OH)HCC_6H_3(OH)(OCH_3)] \end{array}$$

is a reddish-brown powder, m. p. 175-6°, soluble in aqueous sodium hydroxide or carbonate, methyl or ethyl alcohol, and insoluble in water, ether or sodium bicarbonate. It is prepared like the preceding compound by employing vanilline.[706]

3,3′Bis(α-hydroxy-γ-phenylallylamino)-4,4′-dihydroxyarsenobenzene,

$$\begin{array}{l} AsC_6H_3(OH)[NH(OH)HCCH=CHC_6H_5] \\ \| \\ AsC_6H_3(OH)[NH(OH)HCCH=CHC_6H_5] \end{array}$$

results upon refluxing disodium arsphenamine and cinnamic aldehyde in methyl alcoholic solution for two hours in an atmosphere of nitrogen. It is a yellow powder decomposing at 195-200° without melting, slightly soluble in dilute alkalis, acetone, methyl or ethyl alcohol, and insoluble in water, ether or dilute acetic acid. It assumes a reddish-brown color with dilute mineral acids.[705]

A stable solution of a condensation product is also formed upon adding arsphenamine base to an aqueous solution of sulfobenzaldehyde, and warming with sodium hydroxide or carbonate. Upon the addition of alcohol, a yellow sodium salt is precipitated.[427]

Arsphenamine Derivatives.

Sodium 3,3′-diamino-4,4′-dihydroxyarsenobenzene-N-methylenesulinate ("Neoarsphenamine," "Neosalvarsan," "Novarsenobillon," "Neo-

kharsivan," "Novarsenobenzol," "Neodiarsenol," "914" of Ehrlich's series),

$$\begin{array}{l} AsC_6H_3(OH)(NH_2) \\ \| \\ AsC_6H_3(OH)(NH.CH_2OSONa).1CH_3OH \text{ or } 2H_2O \end{array}$$

To an aqueous solution of arsphenamine (25 g. in 250 c.c.) is added 10% aqueous sodium formaldehydesulfoxylate (250 c.c.), and one hour later 10% sodium carbonate solution (80 c.c.). From the resulting liquid, hydrochloric acid (100 c.c. of 12%) precipitates 3,3′-diamino-4,4′-dihydroxyarsenobenzene-N-methylenesulfinic acid, which is then converted into its sodium salt (*neoarsphenamine*) by suspending in water (20 g. in 70-80 c.c.), adding 2N-sodium hydroxide (20 c.c.), and pouring the solution in a thin stream into one liter of alcohol.[707]

The formation of this product is facilitated by operating in solutions of alcohols, particularly methyl or ethyl alcohol, glycol or glycerine. To a solution of arsphenamine (50 parts) in glycol (200 parts) there is added a solution of sodium formaldehydesulfoxylate (31 parts in 50 parts of water), the whole stirred for five minutes, neutralized with sodium carbonate, and finally precipitated with ethyl alcohol, acetone or a mixture of alcohol and ether. This method may be modified by adding sodium carbonate solution (40 c.c. of 12.5%) with stirring to a solution of arsphenamine (25 g.) in glycol (200 c.c.) and 25 c.c. of water. The resulting, finely divided precipitate of arsphenamine base is now treated with an aqueous solution of sodium formaldehyde sulfoxylate (15 g. in 30 c.c.), the whole stirred at 35° until completely dissolved, and the neoarsphenamine precipitated by introducing into a mixture of alcohol and ether.[708]

Neoarsphenamine may also be prepared from 3,3′-dinitro-4,4′-dihydroxyarsenobenzene, 3-nitro or amino-4-hydroxyphenyl arsineoxide or arsonic acid. A solution of 3,3′-dinitro-4,4′-dihydroxyarsenobenzene (100 g.) in sodium hydroxide (60 g. of 40° Bé) and water (1 l.) is warmed with sodium formaldehydesulfoxylate solution (200 g. in 1 liter of water) on a water-bath for two hours, and after cooling and filtering, the free sulfinic acid derivative is first precipitated with dilute sulfuric acid and then converted into the sodium salt.[709]

3-Nitro-4-hydroxyphenylarsineoxide (100 g.) is dissolved in aqueous sodium hydroxide (1 l. of 1.5%), gently warmed for 1-2 hours with an aqueous solution of sodium formaldehydesulfoxylate (200 g. in 1 l.), and the sulfinic acid precipitated with dilute sulfuric acid.[710]

3-Amino-4-hydroxyphenylarsineoxide (10 parts), dissolved in caustic soda (5.7 parts of 40° Bé NaOH in 100 parts of water), is warmed with sodium formaldehydesulfoxylate (10 parts in 50 parts of water) for several hours at 50-60°, and after cooling, the whole is acidified with hydrochloric acid.[710]

Upon warming a solution of sodium 3-nitro-4-hydroxyphenylarsonate

in water (5 parts) with sodium formaldehydesulfoxylate (2 parts in 10 parts of water), the free sulfinic acid slowly separates.[711]

A solution of 3-amino-4-hydroxyphenylarsonic acid (10 parts) in sodium carbonate (2.3 parts in 100 parts of water) is mixed with sodium formaldehydesulfoxylate (20 parts in 100 parts of water) and N-hydrochloric acid (43 parts), and after warming for several hours at 40-60°, the sulfinic acid is precipitated by acidification with dilute sulfuric acid.[711]

Neoarsphenamine is an orange-yellow deliquescent powder, darkening on exposure to air, readily soluble in water or glycerine, but only slightly so in methyl or ethyl alcohol, acetone or ether. Its freshly prepared aqueous solution is yellow in color, reacts neutral toward litmus, decolorizes indigo carmine, and is very sensitive to oxidation,[712] as indicated by its increased toxicity upon exposure to the air. With dilute as well as concentrated mineral acids, or warm acetic acid (36%) it yields precipitates; no visible effects are observed with aqueous sodium hydroxide or carbonate; solutions of barium or calcium hydroxide produce either turbid solutions or faint precipitates. Its behavior with oxidizing agents is similar to that of arsphenamine, while with Millon's reagent a brown precipitate results. Unlike arsphenamine, the neo compound, when boiled with dilute hydrochloric acid, yields a violet coloration upon the addition of Schiff's reagent. The diazotized solution gives with α-naphthylamine hydrochloride and resorcinol color reactions similar to those obtained with arsphenamine. According to Binz,[495] mercuric chloride reacts with an excess of neoarsphenamine, yielding colloidal mercury, 3,3′-diamino-4,4′-dihydroxyarsenobenzene-N-methylenesulfinic acid, the corresponding sulfonic acid derivative,

$$(H_2N)(HO)C_6H_3As = AsC_6H_3(OH)(NH.CH_2OSO_2H),$$

3-amino-4-hydroxyphenylarsineoxide, 3-(iminomethylenesulfonic acid)-4-hydroxyphenylarsineoxide, $OAsC_6H_3(OH)(NH.CH_2OSO_2H)$, and formaldehydesulfonic acid, $CH_2(OH)OSO_2H$.

The analysis of neoarsphenamine always yields lower results for arsenic[713] than that required by the empirical formula,

$$C_{13}H_{13}O_4N_2As_2SNa.1CH_3OH \text{ or } 2H_2O,$$

while those obtained for sulfur are invariably higher. This has been attributed to the presence of varying amounts of the corresponding N,N′-dimethylenesulfinate, uncombined sodium formaldehydesulfoxylate, sodium sulfate and sodium chloride.[714]

Coördination Compounds of Neoarsphenamine.[715]

With Silver Nitrate.—An aqueous solution of silver nitrate (0.77 parts in 100 parts of water) is slowly added with stirring to a concentrated

aqueous solution of neoarsphenamine, and precipitated with alcohol-ether. The product is a black powder dissolving in water to a markedly fluorescent solution.

With Gold Chloride.—A very soluble brownish-red product is obtained by mixing molecular proportions of the constituents in aqueous solution and precipitating with alcohol-ether.

With Platinic Chloride.—A soluble brown powder prepared like the preceding compound.

With Cupric Chloride.—A yellow powder prepared like the gold compound. It gives none of the reactions of ionic copper in the cold, the coördination product decomposing only on boiling.

Disodium 3,3′-diamino-4,4′-dihydroxyarsenobenzene-N,N′-dimethylenesulfinate,

$(NaOSOH_2C.HN)(HO)C_6H_3As = AsC_6H_3(OH)(NH.CH_2OSONa)$,

is prepared by adding a solution of sodium formaldehydesulfoxylate (25 g.) in water (60 c.c.) to an aqueous suspension of arsphenamine base (21 g.), dissolving by gently warming on a water-bath, precipitating the disulfinic acid with concentrated hydrochloric acid (25 c.c.), and converting into the disodium salt in the manner described under neoarsphenamine.[707]

3,3′-Diamino-4,4′-dihydroxyarsenobenzene-N-methylenesulfonic acid, $(H_2N)(HO)C_6H_3As = AsC_6H_3(OH)(NH.CH_2OSO_2H)$.—To a suspension of arsphenamine base (1 part) in water (3 parts) are added successively formaldehyde solution (0.3 parts of 40%) and sodium bisulfite 1 part of 40%, the whole warmed on a water-bath until complete solution results, and the above acid precipitated by the addition of hydrochloric acid.[716] It may also be prepared by adding mercuric chloride (6 g. in 50 c.c. of water) to aqueous neoarsphenamine (50 c.c. of 12%), filtering off the precipitated mercury, introducing successively hydrochloric acid (10 c.c. of 2N) and sodium hypophosphite (3 g.), and allowing to stand for 12 hours.[495] It is a bright yellowish-red powder, which when heated decomposes without melting, sulfurous acid being liberated. It is easily soluble in aqueous alkali hydroxides or carbonates, difficultly so in pure water, and insoluble in alcohol, ether, benzene, acetone or acids.

Its sodium salt (*Sulfarsenol*) is prepared by suspending the free acid in water (3 parts), dissolving by means of aqueous sodium hydroxide or carbonate, and reprecipitating with alcohol or acetone (10-15 volumes) with stirring, or by evaporating a neutral solution of the acid to dryness in vacuo. It forms a reddish-brown powder, dissolving very

easily in water to a stable solution which is claimed to be neutral, but according to Voegtlin,[717] it is slightly acid to litmus. The product is insoluble in strong alcohol, and decomposes without melting when heated. The corresponding potassium and ammonium salts are similarly prepared.[716]

Disodium 3,3′-diamino-4,4′-dihydroxyarsenobenzene-N,N′-dimethylene sulfonate (Sulpharsphenamine),

$$(NaO_2SOCH_2.HN)(HO)C_6H_3As = AsC_6H_3(OH)(NH.CH_2OSO_2Na),$$

is prepared by treating a dilute alcoholic solution of arsphenamine successively with formaldehyde solution (2 or 3 moles) and aqueous sodium bisulfite (4 or 6 moles), and finally precipitating with 95% alcohol. The product is a light yellow precipitate easily soluble in water, and does not decolorize indigo carmine. Its aqueous solution is very stable and does not increase in toxicity on standing in contact with air for 24 hours.[718]

Galyl ("1116" of Mouneyrat's Series).—3-Amino-4-hydroxyphenylarsonic acid (23.3 g.) is dissolved in water (300 c.c.) and caustic soda (90 c.c. of 36° Bé), mixed with 90% alcohol (350 c.c.), the whole cooled and stirred, and phosphorous oxychloride (27 c.c.) introduced. The liquid is then neutralized with caustic soda (18 c.c. of 36° Bé), poured into a solution containing water (1800 c.c.), magnesium chloride (100 g.) and sodium hydrosulfite (500 g.), and finally heated at 50° C. for four hours. The resulting yellow precipitate, consisting of a mixture of *tetrahydroxydiphosphotetraaminodiarsenobenzene*,

$$(HO)OP < \begin{matrix} HN(OH)C_6H_3As = AsC_6H_3(OH)NH \\ HN(HO)C_6H_3As = AsC_6H_3(OH)NH \end{matrix} > PO(OH)$$

and *tetrahydroxymonophosphotetraaminodiarsenobenzene*,

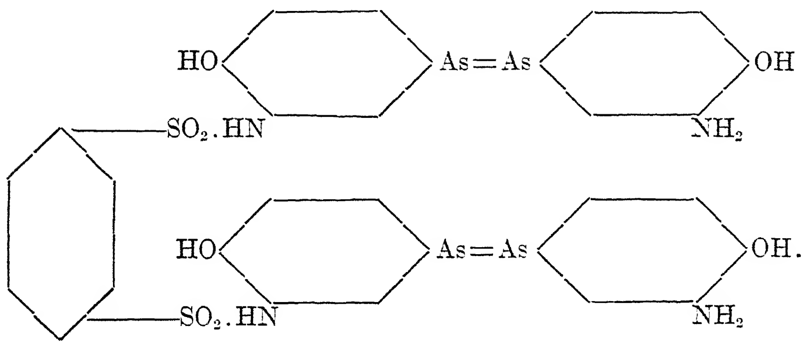
$$\begin{matrix} H_2N(HO)C_6H_3As = AsC_6H_3(OH)NH \\ H_2N(HO)C_6H_3As = AsC_6H_3(OH)NH \end{matrix} > PO(OH),$$

is soluble in dilute sodium carbonate or hydrochloric acid, and reduces Fehling's, Nessler's or Tollens' reagent in alkaline solution.[719]

More recently a "new" Galyl, a sodium salt of the "old" product, was prepared by precipitating a solution of the latter "by means of a solution of sodium hydrosulfite," the resulting compound separating with five molecules of sodium sulfite and containing 18 per cent of arsenic. According to a report of the Council on Pharmacy and Chemistry of the American Medical Association,[720] a solution of the above product responds to practically all the tests for sodium arsphenamine, except that there are present sodium phosphate, sodium sulfite and sugar. The same report also states that the new sodium salt, if present as claimed

by its manufacturer, is easily hydrolyzed into sodium phosphite an sodium arsphenamine; that there is no evidence of a linkage between th sulfite groups and the arsphenamine compound; and that the administra tion of Galyl amounts to the administration of sodium arsephenamine

Benzene-m-3′,3′-disulfamino-bis-3-amino-4,4′-dihydroxyarsenoben zene (Ludyl, "1151" of Mouneyrat's series)



This complex arsenical, prepared from benzene-m-disulfonic chlorid and arsphenamine by the Schotten-Baumann reaction, is a yellow o yellowish-gray powder soluble in aqueous sodium carbonate but in soluble in water. Its sodium salt, precipitated from aqueous solutior by means of alcohol or sodium chloride, dissolves in water with neutral reaction and remains unchanged for several days in the absence of air.[721]

N-Substituted Fatty Acid Derivatives of Arsphenamine.

4,4′-Dihydroxy-3-aminoarsenobenzene-3′-aminoacetic acid,

$(H_2N)(HO)C_6H_3NH.CH_2COOH.$

Prepared by heating a methyl alcoholic suspension of arsphenamine base with aqueous chloroacetic acid at 60-65° in an inert atmosphere, the reaction being accelerated by the addition of potassium iodide. A modification of this procedure consists in employing disodium arsphen-amine and sodium chloroacetate instead of the free acid compounds The product is a yellow powder readily soluble in alkalis or excess of acids, but insoluble in the usual organic solvents.

The sodium salt is prepared by dissolving the acid derivative in concentrated aqueous alkali and either precipitating with alcohol or acetone, or concentrating in vacuo. It is a yellowish-brown powder readily soluble in water to a neutral solution, and insoluble in alcohol or acetone. The potassium and ammonium salts have similar properties but the latter in addition slowly dissociates at ordinary temperature.[72]

4,4'-Dihydroxyarsenobenzene-3,3'-diaminoacetic acid,

$(HOOCH_2C.HN)(HO)C_6H_3As = AsC_6H_3(OH)(NH.CH_2COOH)$,

ay be obtained either from the preceding compound by heating with ueous chloro or bromo acetic acid at 60-65° in an atmosphere of trogen,[723] or from methyl alcoholic disodium arsphenamine, aqueous dium chloroacetate, and a slight amount of copper turnings as a catalyst refluxing for five hours under the same conditions as above, diluting th water, and finally acidifying with dilute hydrochloric acid.[672] The oduct is a yellow powder readily soluble in methyl alcoholic hydroloric acid, aqueous sodium hydroxide, carbonate or bicarbonate, but soluble in water, ether, methyl or ethyl alcohol. It is readily oxidized the corresponding arsonic acid by iodine solution. Its yellowishown disodium salt, $[NaOOCCH_2HN)(HO)C_6H_3As=]_2$, is readily luble in water but insoluble in alcohol or acetone.

4,4'-Dihydroxy-3-aminoarsenobenzene-3'-amino-α-propionic acid,

$$(H_2N)(HO)C_6H_3As = AsC_6H_3(OH)NH.CH\left\langle\begin{matrix}CH_3\\ \\ COOH\end{matrix}\right.,$$

a yellow powder soluble in alkalis or excess of dilute hydrochloric id, insoluble in the usual solvents, and prepared like the corresponding etic acid derivative by employing α-bromopropionic acid.[722] Its yellow dium salt is soluble in water but insoluble in organic solvents.

4,4'-Dihydroxyarsenobenzene-3,3'-diaminopropionic acid,

$$\left.\begin{matrix}H_3C\\ \\ HOOC\end{matrix}\right\rangle HC.HN(HO)C_6H_3As = AsC_6H_3(OH)NH.CH\left\langle\begin{matrix}CH_3\\ \\ COOH\end{matrix}\right..$$

epared like the corresponding diacetic acid derivative without acidifyg the reaction mixture after dilution with water. It is a yellow powder luble in methyl alcohol, aqueous alkali hydroxide, carbonate or bicarmate, dilute hydrochloric or sulfuric acid, insoluble in ether, and is idized to the arsonic acid by iodine.[672]

4,4'-Dihydroxyarsenobenzene-3,3'-diamino-n-butyric acid,

$$\left.\begin{matrix}H_5C_2\\ \\ HOOC\end{matrix}\right\rangle HC.HN(HO)C_6H_3As = AsC_6H_3(OH)NH.CH\left\langle\begin{matrix}C_2H_5\\ \\ COOH\end{matrix}\right.,$$

om disodium arsphenamine and α-bromobutyric acid like the previous mpound, is a yellow powder soluble in methyl alcohol, dilute alkalis acids but insoluble in water.[672]

4,4′-Dihydroxyarsenobenzene-3,3′-diaminoisobutyric acid,

$$\left.\begin{matrix}(H_3C)_2\\HOOC\end{matrix}\right\rangle C.HN(HO)C_6H_3As=AsC_6H_3(OH)NH.C\left\langle\begin{matrix}(CH_3)_2\\COOH\end{matrix}\right.,$$

resembles its isomer.[672] The ethyl ester, prepared from ethyl bromoisobutyrate, is a yellow powder soluble in 95% methyl alcohol, dilute sodium hydroxide or carbonate or ammonia, and insoluble in water, ether, dilute hydrochloric or sulfuric acid. It may be readily hydrolyzed to the corresponding isobutyric acid derivative by warming with concentrated caustic potash in an atmosphere of nitrogen.[672]

4,4′-Dihydroxyarsenobenzene-3,3′-diamino-n-valeric acid,

$$\left.\begin{matrix}H_7C_3\\HOOC\end{matrix}\right\rangle HC.HN(HO)C_6H_3As=AsC_6H_3(OH)NH.CH\left\langle\begin{matrix}C_3H_7\\COOH\end{matrix}\right..$$

A yellow powder soluble in methyl alcohol, sodium hydroxide or carbonate, slightly so in dilute hydrochloric or sulfuric acid, and insoluble in water or aqueous sodium bicarbonate.[672]

The corresponding *isovaleric acid derivative* resembles its isomer except that it is more readily soluble in dilute mineral acids.

4,4′-Dihydroxyarsenobenzene-3,3′-diamino-n-heptylic acid,

$$\left.\begin{matrix}H_{11}C_6\\HOOC\end{matrix}\right\rangle HC.HN(HO)C_6H_3As=AsC_6H_3(OH)NH.CH\left\langle\begin{matrix}C_5H_{11}\\COOH\end{matrix}\right..$$

When the filtrate of the reaction mixture obtained by the usual procedure from disodium arsphenamine and α-bromoheptylic acid is diluted with three volumes of water, a brown resinous mass separates. From this the heptylic acid derivative is isolated by dissolving the dried product in 95% methyl alcohol and precipitating with absolute ether. It forms a yellow powder soluble in methyl alcohol, sodium hydroxide or carbonate, insoluble in sodium bicarbonate, ether or dilute mineral acids.[672]

4,4′-Dihydroxyarsenobenzene-3,3′-diaminostearic acid,

$$\left.\begin{matrix}H_{33}C_{16}\\HOOC\end{matrix}\right\rangle HC.HN(HO)C_6H_3As=AsC_6H_3(OH)NH.CH\left\langle\begin{matrix}C_{16}H_{33}\\COOH\end{matrix}\right.,$$

obtained in small yield upon diluting the filtrate of the reaction mixture with water, exists as a yellow powder having the same solubilities as the preceding compound.[672]

Isomerides of Arsphenamine.

4,4′-Diamino-2,2′-dihydroxyarsenobenzene, is isolated as its dihydrochloride upon reducing 4-amino-2-hydroxyphenylarsonic acid with stannous chloride and concentrated hydrochloric acid at —5° in the presence of glacial acetic acid and a small amount of hydriodic acid. The salt is a bright yellow powder readily soluble in water, from which sodium hydroxide liberates the free base as a yellow precipitate soluble in excess of the reagent. The sulfate is sparingly soluble.[639]

5,5′-Diamino-2,2′-dihydroxyarsenobenzene, a yellow powder soluble in aqueous caustic alkalis or hydrochloric acid, is formed by reducing the corresponding nitrohydroxyarsonic acid with sodium hydrosulfite. When oxidized together with p-xylenol by means of sodium hypochlorite in alkaline solution, it yields an intense cornflower-blue solution of the corresponding iodophenolarsonic acid.[723] A condensation product with sodium benzaldehydesulfonate results upon allowing the components to stand in slightly alkaline solution in the absence of air, and precipitating with alcohol.[427]

2,2′-Diamino-3,3′-dihydroxyarsenobenzene, lustrous leaflets melting with decomposition at 205-8°, is obtained by reducing the corresponding nitrohydroxyarsonic acid with sodium hydrosulfite at ordinary temperature.[704]

4,4′-Diamino-3,3′-dihydroxyarsenobenzene, may be obtained by reducing 4-amino-3-hydroxyphenylarsonic acid with sodium hydrosulfite at 60-65°.[725] Another method consists in diazotizing 3-nitro-4-aminophenylarsonic acid, treating with sodium acetate to replace the nitro group by hydroxyl, coupling with β-naphthol in alkaline solution, dissolving the resulting dye, $H_2O_3As.C_6H_3(OH).N=N.C_{10}H_6.OH$, in water containing sodium hydroxide and acetate, and finally warming with sodium hydrosulfite at 35-8° until complete decolorization occurs. The solution is now cooled to 10°, the precipitated 1-amino-2-naphthol filtered off, the remainder precipitated from the filtrate by saturating with carbon dioxide, and the final filtrate warmed for two hours at 65-70°, when the above arseno compound gradually separates out.[726]

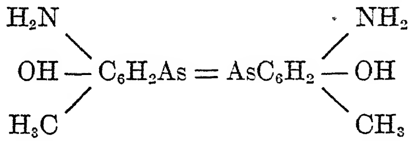
The product is a yellow, readily oxidizable powder, scarcely soluble in water, but easily so in dilute alkalis or mineral acids. The dihydrochloride, prepared by dissolving the base in alcoholic hydrochloric acid and precipitating with ether in the absence of air, is a pale yellow powder easily soluble in water, the free base being reprecipitated by the addition of sodium carbonate or acetate. It diazotizes to an intensely yellow colored diazo compound yielding a splendid blue azo color when coupled with 1-amino-8-hydroxynaphthalene-4-sulfonic acid in alkaline

solution. The sparingly soluble sulfate, $[H_2SO_4.H_2N.C_6H_3(OH)As=]_2$, is prepared by adding sulfuric acid or an alkali sulfate to a solution of the dihydrochloride.

2,2′ or 6,6′-Diamino-5,5′ or 3,3′-dihydroxyarsenobenzene is similarly prepared.[727]

Homologues of Arsphenamine.

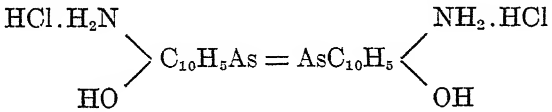
3,3′-Diamino-4,4′-dihydroxy-5,5′-dimethylarsenobenzene,



prepared by reducing the corresponding nitro arsonic acid with sodium hydrosulfite, is a pale yellow powder melting at 165-7° with decomposition, easily soluble in alkalis or dilute hydrochloric acid, but only sparingly in water or organic solvents. Its dihydrochloride, a pale yellow powder containing two molecules of water, is readily soluble in water or methyl alcohol, less so in ethyl alcohol, and practically insoluble in ether or acetone.[728]

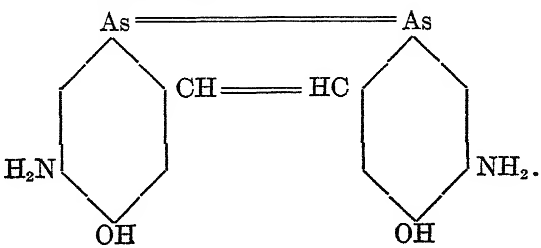
3,3′-Diamino-4,4′-dihydroxy-6,6′-dimethylarsenobenzene is similarly prepared.[729]

3,3′-Diamino-4,4′-dihydroxy-α-arsenonaphthalene dihydrochloride,



is a brownish-yellow, insoluble powder obtained by reducing the corresponding nitro arsonic acid with stannous chloride and hydrochloric acid in methyl alcoholic solution.[590]

5,5′-Diamino-4,4′-dihydroxy-1,1′-arseno-2,2′-stilbene,



Obtained by reducing the corresponding dinitrodihydroxystilbenediarsonic acid with either sodium hydrosulfite in alkaline solution, or with stannous chloride and hydrochloric acid containing a slight amount of potassium iodide. It is a yellowish-brown powder readily soluble in caustic soda but insoluble in acids.[730]

B. Secondary Derivatives.

1. *Diaryl Arsines*, R_2AsH.—The fact that, up to the present time, diphenylarsine is the only known member of this class of arsenicals may probably be accounted for by the many difficulties involved in their preparation, purification and preservation.

Diphenylarsine, $(C_6H_5)_2AsH$.—Diphenylarsinic acid is mixed with an excess of amalgamated zinc dust covered with a layer of ether, and reduced by the gradual addition of concentrated hydrochloric acid accompanied by vigorous agitation. When the reaction is completed, the ethereal solution is dried over fused calcium chloride and distilled in an atmosphere of carbon dioxide. Throughout the process it is very essential that air or moisture be excluded.

The product is a clear, colorless oil boiling at 174°/25 mm., and possessing an odor resembling that of phenylarsine, but less pleasant. Its concentrated vapor produces catarrhal symptoms and sneezing. It is soluble in alcohol, ether or other organic solvents but insoluble in water. When exposed to the air the arsine is instantly oxidized to a white, or faintly yellow, hard mass consisting of diphenylarsinic acid and some diphenylarsineoxide. With bromine or iodine it yields the corresponding halogenated diphenylarsine: [43]

$$(C_6H_5)_2AsH + X_2 \longrightarrow (C_6H_5)_2AsX + HX.$$

When heated for three hours at 295° it decomposes according to the equations:

$$\begin{cases} 6(C_6H_5)_2AsH \longrightarrow 4(C_6H_5)_3As + 2As + 3H_2 \\ 2(C_6H_5)_3As \longrightarrow 3C_{12}H_{10} + 2As. \end{cases}$$ [262]

2. *Secondary Halogenated, Cyano and Thiocyano Arsines*, R_2AsX, R_2AsCN, R_2AsCNS.—The secondary aromatic halogenated arsines are of particular importance because they serve as the starting materials for the preparation of many other arsenicals as, for example, diaryl arsineoxides, -arsinic acids, -cyanoarsines, esters of diarylarsenious acids or diarylarsinetrihalides. During the recent war diphenylchloro- and cyanoarsines were manufactured on a large scale for military purposes. The English method of preparing the chloro compound depended upon the interaction of diphenylamine and arsenic trichloride, while according to the German procedure aniline was converted into benzene dia-

zonium chloride, the latter condensed with sodium arsenite to disodium phenylarsonate, which in turn was reduced to phenylarsenious acid by means of sodium sulfite. By condensing this arsenious acid with benzene diazonium chloride, diphenylarsinic acid was obtained, which on reduction with sulfur dioxide in hydrochloric acid solution yielded diphenylchloroarsine.

In addition to the above methods, the purely aromatic or aromatic-aliphatic secondary halogenated arsines may be obtained:

1. On heating triarylarsine dihalides at 160-200°, or by distilling under reduced pressure:

$$R_3AsX_2 \longrightarrow R_2AsX + RX.$$

If the tertiary arsinedihalide contains one aryl and two alkyl radicals there is formed an aromatic-aliphatic halogenated arsine together with one molecule of alkyl halide.

2. From secondary arsineoxides by heating with concentrated haloid acids:

$$[R_2As]_2O + 2HX \longrightarrow 2R_2AsX + H_2O.$$

3. By heating aryl dihalogenated arsines with mercury diaryls:

$$2RAsX_2 + Hg\ R'_2 \longrightarrow 2RR'AsX + HgX_2.$$

4. When tetraaryldiarsines are treated with halogens in the presence of a solvent such as benzene:

$$R_2As - AsR_2 + X_2 \longrightarrow 2R_2AsX.$$

5. From triarylarsines and arsenic trihalides at high temperatures:

$$2R_3As + AsX_3 \longrightarrow 3R_2AsX.$$

In this method a dihalogenated arsine is also obtained, a portion of which may react with the tertiary arsine to form the secondary compound:

$$R_3As + RAsX_2 \longrightarrow 2R_2AsX.$$

6. When arylmagnesium halides react with arsenic trihalides according to the equation:

$$2RMgX + AsX_3 \longrightarrow R_2AsX + 2MgX_2.$$

7. By the interaction of iodine with secondary arsines:

$$R_2AsH + I_2 \longrightarrow R_2AsI + HI.$$

8. Upon reducing arsinic acids with concentrated hydriodic acid and red phosphorus.

9. For the preparation of aromatic-aliphatic halogenated arsines, aryl arsineoxides are treated with alkyl halides in alcoholic sodium hydroxide solution, acidified, potassium iodide added, and the whole saturated with sulfur dioxide.

The unsubstituted halogenated compounds are practically all colorless or yellow, transparent, oily liquids which are very irritating to the nasal mucous membrane. They are generally insoluble in water, soluble in organic solvents, and are converted into the corresponding arsineoxides by means of alkalis—very slowly in aqueous solution but much more rapidly in alcoholic medium. With halogens they combine to form the corresponding diarylarsinetrihalides. When heated with alkyl iodides in a sealed tube, dialkyldiarylarsonium triiodides are produced:

$$R_2AsX + 2R'X \longrightarrow R_2R'_2AsX_3.$$

They react with sodium alkoxides forming arylalkoxyhalogenated arsines:

$$R_2AsX + NaOR' \longrightarrow R(R'O)AsX \quad (R = \text{an aryl and } R' \text{ an alkyl radical}).$$

The nuclear substituted halogenated arsines are crystalline solids possessing the same general properties as the unsubstituted derivatives, except that they react more readily with aqueous alkalis, forming either the arsineoxide or the alkali salt of diarylarsenious acid:

$$2R_2AsX + Na_2CO_3 \longrightarrow (R_2As)_2O + 2NaX + CO_2$$
$$R_2AsX + 2NaOH \longrightarrow R_2AsONa + NaX + H_2O.$$

The secondary aromatic cyano- and thiocyanoarsines are closely related to the halogenated arsines, from which they can be readily obtained by treatment with alkali cyanides and thiocyanides respectively. Mixed aliphatic-aromatic cyanoarsines may also be prepared by decomposing aryldialkylarsine cyanobromides, the smallest alkyl group splitting off with the halogen, e. g.,

$$(C_6H_5)(CH_3)(C_2H_5)As.CN.Br \longrightarrow (C_6H_5)(C_2H_5)As.CN + CH_3Br.$$

Both the cyano- and thiocyano- compounds are characterized by the readiness with which the -CN and -CNS radicals may be eliminated by the action of water.

Phenylmethylchloroarsine, $(C_6H_5)(CH_3)AsCl$, is prepared by heating phenyldimethylarsine dichloride in an oil-bath at 180° for one-half hour,[731] or from phenylmethyliodoarsine by treating with a calculated amount of caustic soda, and shaking the resulting arsineoxide repeatedly with small quantities of concentrated hydrochloric acid.[732] It is a pale yellow liquid resembling phenyldichloroarsine both in appearance and physiological properties, and boiling at 229-32°, 113.5°/14 mm. When heated with methyl iodide in a sealed tube at 100° for two hours, it forms phenyltrimethylarsonium triiodide.[733]

Phenylmethylbromoarsine, similarly prepared from phenyldimethylarsine dibromide, is a colorless liquid, b. p. 250°.[734]

Phenylmethyliodoarsine.—Upon the addition of methyl iodide to a well-cooled solution of phenylarsineoxide in alcoholic sodium hydroxide, a vigorous reaction occurs, which is allowed to proceed to completion over night. The reaction mixture is then acidified, the alcohol removed by distillation, potassium iodide added, and the whole saturated with sulfur dioxide, when the iodoarsine separates as a dark oil which is purified by drying over calcium chloride and subsequently distilling.[732] Another method of preparation consists in adding methyl iodide to a solution of phenyldichloroarsine in alcoholic sodium hydroxide and permitting the reaction to continue for 24 hours. The product is then neutralized with hydrochloric acid, filtered to remove any sodium chloride, and the alcohol in the filtrate distilled off. Finally, the residue is dissolved in water, acidified with hydrochloric acid and saturated with sulfur dioxide.[265] It may also be obtained by gradually adding phenylmethylchloroarsine to a solution of sodium iodide in dry acetone.[733] The compound is a golden-yellow, oily liquid, b. p. 138-40°/12 mm., 143-4°/17-8 mm.; soluble in organic solvents but not in water. Heated with methyl iodide in a sealed tube at 100° for two hours, it forms phenyltrimethylarsonium triiodide.

Phenylethylchloroarsine, $(C_6H_5)(C_2H_5)AsCl$, prepared from phenyldiethylarsine dichloride by heating at 160-80° for twenty minutes in an open flask, is a colorless, highly refractive liquid, b. p. 249° with decomposition.[735]

The corresponding *bromoarsine* is obtained when phenyldiethylarsine dibromide is heated at 200° in a current of carbon dioxide. It is a practically colorless liquid which upon distillation under atmospheric pressure decomposes to a black tar.[735]

Phenylethoxychloroarsine, $(C_6H_5)(C_2H_5O)AsCl$.—Sodium ethoxide is gradually added to phenyldichloroarsine, and the mixture heated on the water-bath for two and one-half hours:

$$C_6H_5AsCl_2 + NaOC_2H_5 \longrightarrow (C_6H_5)(C_2H_5O)AsCl + NaCl.$$

The product is a colorless oil boiling at 125-6°/12 mm., and gradually hydrolyzing in water to a white solid which crystallizes from petroleum in needles, m. p. 127-30°. It is interesting to note that this product has a higher melting point than that ascribed to phenylarsineoxide.[736]

Diphenylchloroarsine, $(C_6H_5)_2AsCl$.—Mercury diphenyl is heated with an excess of phenyldichloroarsine in a reflux apparatus on a sand bath at 320° for 5-10 minutes, and the resulting dark liquid decanted

and fractionated. The fraction boiling above 300° is maintained in a current of carbon dioxide at a temperature slightly below its boiling point for some time to insure the complete removal of any unchanged phenyldichloroarsine. The greater part of the remaining liquid distills over at 333° and consists of pure diphenylchloroarsine.[737, 738] The same product results upon converting triphenylarsine into its dichloride, distilling under 13-14 mm. pressure, and separating the diphenylchloroarsine and chlorobenzene by fractionation.[739] It is also obtained, together with phenyldichloroarsine, by heating triphenylarsine with arsenic trichloride at temperatures ranging between 250 and 350° under atmospheric pressure: [740, 741]

$$\left\{\begin{array}{l}(C_6H_5)_3As + 2AsCl_3 \longrightarrow 3C_6H_5AsCl_2 \\ 2(C_6H_5)_3As + AsCl_3 \longrightarrow 3(C_6H_5)_2AsCl \\ C_6H_5AsCl_2 + (C_6H_5)_3As \longrightarrow 2(C_6H_5)_2AsCl.\end{array}\right.$$

Other methods consist in gradually adding phenylmagnesium bromide to a large excess of arsenic trichloride in the presence of ether,[742] or in treating diphenylarsineoxide with hydrochloric acid.[743, 744]

The following procedure for large scale production was developed in Germany during the recent war. Aniline is dissolved in the requisite amount of hydrochloric acid, diazotized with sodium nitrite at 0-5°, and the resulting benzene diazonium chloride converted into disodium phenylarsonate by condensation with sodium arsenite:

$$C_6H_5N_2Cl + Na_3AsO_3 \longrightarrow C_6H_5AsO_3Na_2 + NaCl + N_2.$$

This is first transformed into the free arsonic acid by neutralization with hydrochloric acid, and then reduced to phenyldihydroxyarsine (phenylarsenious acid) by means of sodium sulfite:

$$C_6H_5AsO_3H_2 + Na_2SO_3 \longrightarrow C_6H_5As(OH)_2 + Na_2SO_4.$$

After dissolving in caustic soda, the dihydroxyarsine is condensed with benzene diazonium chloride to form the sodium salt of diphenylarsinic acid, which is then neutralized with hydrochloric acid, yielding the free arsinic acid:

$$C_6H_5As(ONa)_2 + C_6H_5N_2Cl \longrightarrow (C_6H_5)_2AsO.ONa + NaCl + N_2.$$

By dissolving in three volumes of hydrochloric acid and introducing an excess of sulfur dioxide, the diphenylarsinic acid is converted into the chloroarsine, with the intermediate formation of the arsineoxide:

$$\left\{\begin{array}{l}2(C_6H_5)_2AsO.OH + 2SO_2 + H_2O \longrightarrow [(C_6H_5)_2As]_2O + 2H_2SO_4. \\ [(C_6H_5)_2As]_2O + 2HCl \longrightarrow 2(C_6H_5)_2AsCl + H_2O.\end{array}\right.$$

The oily product is finally heated under reduced pressure to remove moisture and hydrochloric acid.[745]

The English method of preparation originally consisted in heating diphenylamine with arsenic trichloride, but this procedure was subsequently improved so that arsenic trioxide could be employed instead of the trichloride. Fused diphenylamine is first converted into the hydrochloride by heating with 1.1 moles of hydrochloric acid (d, 1.18) with continuous agitation until the water has been almost entirely eliminated, and the residual white powder dried at 50-60° and fused with arsenic trioxide, while stirring continuously. When fusion is complete, the heating and stirring are continued for four more hours, during which time the temperature gradually rises to 200°. The reaction is regarded as completed when the evolution of water vapor ceases.[746]

Diphenylchloroarsine is a pale yellow, oily liquid, b. p. 333° in a current of carbon dioxide, 230°/13-14 mm.; d, 1.42231/15°; does not fume in air, and has a faint odor at ordinary temperature which becomes very irritating when heated. According to Norris, however, it has a disagreeable odor, causing sneezing and temporary illness.[745] It is soluble in absolute alcohol, ether or benzene, difficultly in aqueous caustic alkalis and insoluble in water, ammonia or sodium carbonate solution. With chlorine or bromine it combines additively, forming the corresponding diphenylarsinetrihalides, while continued boiling with concentrated nitric acid oxidizes it to diphenylarsinic acid. Heated with methyl iodide in a sealed tube at 100° for three hours, the chloroarsine yields diphenyldimethylarsonium triiodide and diphenyliodoarsine.[747]

Diphenylbromoarsine is made from the corresponding arsineoxide by heating with fuming hydrobromic acid in a sealed tube,[748, 749, 750] or by heating triphenylarsine with arsenic tribromide at 300-50° for three hours.[749] According to LaCoste and Michaelis it is a yellow, oily liquid boiling at 356°, but both Pope and Steinkopf claim it to be a practically colorless crystalline solid melting at 54-6°. Heated with methyl iodide for six hours at 100° it yields methyl bromide, diphenyliodoarsine and diphenyldimethylarsonium triiodide.

Diphenyliodoarsine was first obtained as a deep red olive by Dehn,[751] who heated diphenylarsine in a sealed tube with slightly less than two moles of iodine in ethereal solution. More recently it has been prepared by heating diphenylarsineoxide with fuming hydriodic acid in a sealed tube for two hours at 100°; also from triphenylarsine by heating with arsenic triiodide at 350-60° for six hours.[749] Another method consists in adding diphenylchloroarsine to an anhydrous acetone solution of sodium iodide, allowing to stand for 24 hours, filtering off the sodium chloride, and removing the solvent from the filtrate by evaporation. The residual oil is taken up with ether, filtered, the solvent evaporated off from the filtrate, and crystallization effected by adding a few crystals of pure diphenyliodoarsine.[750]

According to Pope[749] the compound crystallizes from benzene in yellow crystalline scales, m. p. 45-6°; b. p. 204-18°/18 mm., while Steinkopf's product[750] crystallizes from absolute alcohol in lustrous, yellow, transparent, hexagonal crystals, m. p. 40.5°; readily soluble in ether, acetone, benzene, chloroform, carbon bisulfide or carbon tetrachloride and insoluble in water. Heated with methyl iodide in a sealed tube at 100° for five hours, it forms diphenyldimethylarsonium triiodide.

Phenyl-p-tolylchloroarsine, $(C_6H_5)[C_6H_4(CH_3)]AsCl$.—On boiling a mixture of 30 g. of mercury-di-p-tolyl and 180 g. of phenyldichloroarsine for five hours, cooling and mixing the decanted, supernatant liquid with anhydrous petroleum ether, there occurs a separation of mercury-p-tolyl-chloride as a dark brown oil which subsequently solidifies. This is filtered off, the filtrate first warmed on a steam-bath to remove petroleum ether, and then subjected to fractional distillation in a current of carbon dioxide, the unchanged phenyldichloroarsine distilling over up to 300°. In order to prevent decomposition, the secondary chloroarsine is then obtained by continuing the distillation under reduced pressure—at 29 mm. it distills between 215 and 237°, at 50 mm. between 215 and 240°. It is a colorless, oily, non-fuming liquid unaffected by moisture. With chlorine it forms the corresponding arsinetrichloride; with alcoholic potash, the arsineoxide.[752]

Di-(p-tolyl) chloroarsine, $(CH_3.C_6H_4)_2AsCl$, is made by boiling mercurydi-p-tolyl with 3-4 parts of 4-methylphenyldichloroarsine in a reflux apparatus,[753] or by distilling tri-p-tolylarsine dichloride under reduced pressure.[754] According to Michaelis the product consists of colorless crystals, m. p. 45°; b. p. 340-5°, while according to LaCoste it is a pale yellow oil which cannot be crystallized. With dry chlorine it forms the arsinetrichloride.

Di-α-naphthylchloroarsine, $(C_{10}H_7)_2AsCl$, is obtained by gradually adding α-naphthylmagnesium bromide to a large excess of arsenic trichloride in the presence of ether.[742]

Di(3-nitrophenyl) chloroarsine, $(O_2N.C_6H_4)_2AsCl$.—Chlorine is introduced into a suspension of tetra(3-nitrophenyl)diarsine in benzene until complete solution results, and the unstable di(nitrophenyl)arsinetrichloride thus obtained converted into the chloroarsine by mixing with an excess of the above diarsine. It forms pale yellow needles, m. p. 112°; readily soluble in benzene or chloroform, sparingly in ether, and yields the corresponding hydroxyarsine on boiling with water. The chloroarsine readily dissolves in alkalis, excepting ammonia, forming salts of di(nitrophenyl) arsenious acid.[743]

Di(3-nitrophenyl)bromoarsine, prepared like the chloro compound, consists of colorless transparent leaflets, m. p. 93°. With bromine in benzene solution it forms the corresponding arsinetribromide.[743]

Di(3-aminophenyl)chloroarsine hydrochloride,

$$[(HCl.H_2N)C_6H_4]_2AsCl.$$

Obtained from the corresponding arsineoxide by treatment with concentrated hydrochloric acid. It forms colorless needles extremely soluble in water, and is converted into the arsineoxide by means of sodium carbonate.[755]

Di(4-methoxyphenyl)chloroarsine, [*Di-p-anisylchloroarsine*],

$$(CH_3O.C_6H_4)_2AsCl,$$

from the corresponding arsineoxide by treating with concentrated hydrochloric acid, crystallizes from ether in pale yellow needles, m. p. 79-80°; readily soluble in ether, less so in alcohol. It is converted into the arsineoxide by caustic soda.[756]

The corresponding *iodoarsine*[756] is a heavy red oil obtained by warming tri-p-anisylarsine with hydriodic acid (d, 1.56):

$$(CH_3O.C_6H_4)_3As + HI \longrightarrow (CH_3O.C_6H_4)_2AsI + C_6H_5.OCH_3.$$

Di(4-carboxyphenyl)iodoarsine [*Di-p-benzarsenious iodide*],

$$(HOOC.C_6H_4)_2AsI,$$

prepared by heating the corresponding arsinic acid with concentrated hydriodic acid and red phosphorus, is a yellowish-white, ill-defined crystalline mass melting above 280°; soluble in alcohol, ether or chloroform. When boiled with water it decomposes yielding hydriodic acid.[757]

Di(3-amino-4-hydroxyphenyl)chloroarsine hydrochloride,

$$[(HCl.H_2N)(HO)C_6H_3]_2AsCl.$$

Di(3-nitro-4-hydroxyphenyl)arsinic acid is dissolved in dilute caustic soda, reduced with sodium hydrosulfite at 60° in an atmosphere of carbon dioxide, and the resulting gray powder dissolved in methyl alcohol-hydrochloric acid, filtered and finally reprecipitated with concentrated hydrochloric acid. The above salt forms lustrous leaflets, m. p. 215°; readily soluble in water or methyl alcohol, sparingly in concentrated hydrochloric acid.[758]

Phenylchloroarsinoacetic acid, $\begin{matrix} C_6H_5 \\ HOOCCH_2 \end{matrix}\Big\rangle AsCl$, is made by dissolving phenylarsinoacetic acid in concentrated hydrochloric acid, adding

a few crystals of potassium iodide and saturating with sulfur dioxide. It crystallizes in plates melting at 102-3°, and yields phenyldichloroarsine with phosphorus pentachloride in chloroform solution. The corresponding *bromo compound*, similarly prepared by employing hydrobromic acid, melts at 113-14°.[759]

Phenylbromoarsinoacetanilide, $\begin{matrix} C_6H_5 \\ C_6H_5NH.COCH_2 \end{matrix}\!\!>\!AsBr$, is prepared from phenylarsinoacetanilide like the preceding compound. After recrystallization from methyl alcohol it melts at 108-10°.[760]

Phenylethylcyanoarsine, $(C_6H_5)(C_2H_5)As.CN$, results upon heating phenylmethylethylarsine with cyanogen bromide. The corresponding arsine cyanobromide forms at first, but is immediately decomposed into methyl bromide and the above cyanoarsine, b. p. 148-50°/23 mm.[761]

Phenyl-n-propylcyanoarsine, similarly prepared from phenylmethyl-n-propylarsine, boils at 150-55°/20 mm.[762]

Diphenylcyanoarsine, $(C_6H_5)_2As.CN$, was manufactured on a large scale in Germany by vigorously stirring dephenylchloroarsine with a saturated aqueous solution of sodium or potassium cyanide at 60°: [763]

$$(C_6H_5)_2AsCl + NaCN \longrightarrow (C_6H_5)_2As.CN + NaCl.$$

It may also be obtained from diphenylarsineoxide by treating with anhydrous hydrocyanic acid either at ordinary temperature,[736] or by heating in a sealed tube at 100° for two hours; [764] or by allowing it to react with 90 per cent hydrocyanic acid for 24 hours.[765]

$$[(C_6H_5)_2As]_2O + 2HCN \longrightarrow 2(C_6H_5)_2As.CN + H_2O.$$

Other methods consist in heating diphenylethoxyarsine in a current of dry hydrocyanic acid at 140° for three hours; [736] heating diphenylchloroarsine with an excess of freshly prepared, dry silver cyanide at 150-60° for three hours:

$$(C_6H_5)_2AsCl + AgCN \longrightarrow (C_6H_5)_2As.CN + AgCl;$$

heating diphenylarsinesulfide with mercuric cyanide at 160-200° or with silver cyanide at 160°:

$$[(C_6H_5)_2As]_2S + \begin{cases} Hg(CN)_2 \\ 2AgCN \end{cases} \longrightarrow 2(C_6H_5)_2As.CN + \begin{cases} HgS \\ Ag_2S, \end{cases}$$

or reacting tetraphenyldiarsine with mercuric cyanide at 250°: [765]

$$(C_6H_5)_2As—As(C_6H_5)_2 + Hg(CN)_2 \longrightarrow 2(C_6H_5)_2As.CN + Hg.$$

The cyanoarsine crystallizes in almost colorless plates, m. p. 35° (Sturniolo), 30-4° (McKenzie), 28-30° (Morgan), 31.5° (Steinkopf); b. p. 200-1°/13.5 mm. (Steinkopf), 213°/21 mm. (McKenzie). It possesses an odor resembling both garlic and bitter almonds, and is very irritating to the nasal mucous membrane, inducing sneezing. Moist air attacks it liberating hydrocyanic acid. It is converted into the corresponding arsineoxide by distilling either in a current of steam or under reduced pressure (100 mm.), by heating with water, or by treating with caustic alkalis. Heating with concentrated nitric acid on a water-bath, or treatment at ordinary temperature with either hydrogen peroxide (2 per cent) or bromine water, causes oxidation of the cyanoarsine to diphenylarsinic acid.[766] On passing chlorine into a benzene solution of the cyanoarsine, a solid, probably $[(C_6H_5)_2AsCl_2]_2O$, is obtained which fumes in air, melts indefinitely at about 115°, and dissolves in boiling water, yielding needles of diphenylarsinic acid upon cooling. From the filtrate of the above oxychloride a crystalline deposit of diphenylcyanoarsine dichloride, $(C_6H_5)_2As.CN.Cl_2$, m. p. 130-3°, is gradually formed. When heated with methyl iodide in a sealed tube at 100° for six hours the cyanoarsine yields diphenyldimethylarsonium iodide and -triiodide, together with a very slight amount of an unidentified compound melting at 160-8°.

Diphenylarsinoformamide, $(C_6H_5)_2As.CONH_2$, is precipitated upon thoroughly shaking diphenylcyanoarsine with dilute hydrogen peroxide, rendering alkaline and gently warming:

$$(C_6H_5)_2As.CN + H_2O_2 \longrightarrow (C_6H_5)_2As.CONH_2 + O.$$

By diazotizing in dilute sulfuric acid and warming the resulting solution, it is converted into diphenylarsinoformic acid, $(C_6H_5)_2As.COOH$:

$$(C_6H_5)_2As.CONH_2 + HNO_2 \longrightarrow (C_6H_5)_2As.COOH + N_2 + H_2O.$$

The latter may be also obtained directly from diphenylcyanoarsine by boiling for 12 hours with 1:1 sulfuric acid, cooling and isolating through the barium salt.[224]

Diphenylthiocyanoarsine, $(C_6H_5)_2As.CNS$. — The corresponding chloroarsine is allowed to react with sodium thiocyanate in acetone solution for about thirty minutes and then worked up like cacodyl thiocyanate. It is a liquid with a faint brown color, probably due to slight decomposition; b. p. 230-3°/22-3 mm.; miscible in all proportions with benzene or acetone. Water causes the elimination of the CNS radical, leaving an unidentified solid.[731] By heating with methyl iodide in a sealed tube at 100° for six hours, the thiocyanoarsine yields diphenyldimethylarsonium triiodide and diphenyliodoarsine.[767]

3. *Diaryl Arsineoxides and Hydroxyarsines (Diaryl Arsenious Acids)*, $(R_2As)_2O$ and $R_2AS.OH$.—The compounds described in this chapter are more stable than the corresponding aliphatic derivatives due to the presence of the more negative aryl radicals. Although the unsubstituted hydroxyarsines, with the exception of the dibenzyl compound, can only be isolated in the form of esters, stable derivatives may be obtained by introducing into the ring negative substituents, such as nitro or carboxyl groups. Both the arsineoxides and hydroxyarsines are generally crystalline compounds, with the exception of methylphenyl- and phenyl-p-tolylarsineoxides, which are liquids. They are insoluble in water, and are converted into the corresponding monohalogenated arsines by concentrated haloid acids. The oxides result from the interaction of diaryl monohalogenated arsines and alkalis:

$$2R_2AsX + 2KOH \longrightarrow (R_2As)_2O + 2KX + H_2O \text{ (X = a halogen atom).}$$

The hydroxyarsines may be obtained either by the same method according to the equation:

$R_2AsX + KOH \longrightarrow R_2As.OH + KX$ (when R contains negative substituents), or by the mild reduction of the corresponding diaryl arsinic acids:

$$R_2AsO.OH + H_2 \longrightarrow R_2As.OH + H_2O.$$

Phenylmethylarsineoxide, $[(C_6H_5)(CH_3)As]_2O$, results upon warming the corresponding bromoarsine with potassium hydroxide in alcoholic solution. It is a practically colorless, strongly refractive oil, b. p. 94°/11 mm.; soluble in alcohol and only very slightly so in water.[768]

Diphenylarsineoxide, $[(C_6H_5)_2As]_2O$.—Prepared by warming diphenylchloroarsine with either alcoholic potash,[769] or aqueous sodium hydroxide;[770] or from phenylmagnesium bromide and arsenic trioxide in ether medium.[771] It crystallizes in warty aggregates melting at 91-2° (LaCoste), 89-91° (Pope), 92.5-93.5° (McKenzie), and volatilizing at higher temperatures with partial decomposition. It combines additively with chlorine, forming the corresponding oxychloride, while with phosphorous acid in alcoholic solution it yields tetraphenyldiarsine.[511]

The *ethyl ester of diphenylarsenious acid (Diphenylethoxyarsine)*, $(C_6H_5)_2As.OC_2H_5$, results upon heating diphenylchloroarsine with sodium ethoxide on a water-bath for one hour.[736] The *phenyl ester (Diphenylphenoxyarsine)*, $(C_6H_5)_2As.OC_6H_5$, derived from sodium phenolate and diphenylchloroarsine in xylene solution, is a colorless liquid, sp. gr. 1.3113/11°; b. p. 230-1°/15 mm. It cannot be solidified by freezing, and, unlike the isomeric triphenylarsineoxide, is completely hydrolyzed by boiling water. It combines additively with halogens alone, in marked contrast to the corresponding phosphorus compound, $(C_6H_5)_2P.OC_6H_5$, which unites with oxygen, sulfur, selenium or methyl iodide.[772] The free acid is too unstable to be isolated.

Phenyl-p-tolylarsineoxide, $[C_6H_5(C_6H_4.CH_3)As]_2O$, is a pale yellow, syrupy liquid which cannot be solidified. With chlorine it forms the corresponding oxychloride.[773]

Di-p-tolylarsineoxide, $[(C_6H_4.CH_3)_2As]_2O$.—Colorless silky needles from ether melting at 98°, and yielding tri-p-tolylarsine on heating.[753]

Dibenzyl hydroxyarsine or *-arsenious acid,* $(C_6H_5.CH_2)_2As.OH$, is obtained on warming benzylmagnesium bromide and arsenic trioxide in ethereal solution. It separates in the form of lustrous needles melting at 214° and practically insoluble in ether, but when recrystallized from alcohol it crystallizes in leaflets, m. p. 215-6°.[774]

Di(3-nitrophenyl) hydroxyarsine or *-arsenious acid,*

$$(O_2N.C_6H_4)_2As.OH.$$

White felted needles from alcohol, m. p. 149°; prepared from the corresponding chloroarsine and alkali. The compound, which reduces silver nitrate, is unaffected by heating at 110° for three hours, but is gradually decomposed with darkening at higher temperatures. Despite the stability of the free acid, its salts are very unstable.[775]

Di(4-nitrophenyl) arsenious acid results upon reducing the corresponding arsinic acid with hydriodic acid in glacial acetic acid solution. The product intumesces upon heating, is insoluble in water, alcohol or aqueous sodium carbonate, but readily dissolves in glacial acetic acid or caustic soda.[776]

Di(3-aminophenyl) arsineoxide, $[(H_2N.C_6H_4)_2As]_2O$, obtained from the corresponding dinitroarsinic acid by reduction with powdered iron and a slight amount of ferric chloride in boiling water, is insoluble in alkali, and yields the dihydrochloride of the corresponding chloroarsine with concentrated hydrochloric acid.[755]

Di(4-methoxyphenyl) arsineoxide [*Di-p-anisylarsineoxide*],

$$[(CH_3O.C_6H_4)_2As]_2O,$$

has been indirectly obtained from tri-p-anisylarsine by warming with hydriodic acid, and heating the resulting mixture of di-p-anisyliodoarsine and anisole with aqueous caustic soda. When recrystallized from alcohol or benzene the product melts at 130°.[756]

Di(4-carboxyphenyl) hydroxyarsine [*Di-p-benzarsenious acid*],

$$(HOOC.C_6H_4)_2As.OH,$$

is a white crystalline precipitate obtained by dissolving the corresponding iodoarsine in aqueous sodium carbonate and precipitating with

·drochloric acid. It is readily soluble in alcohol but sparingly in ıter or dilute mineral acids. Its calcium salt,

$$HO.As[(C_6H_4.COO)_2]Ca.2H_2O,$$

a white pulverulent precipitate.[777]

4. *Diaryl Arsinesulfides,* $(R_2As)_2S$.—Compounds of this type may prepared:

1. From diaryl monohalogenated arsines by treatment with sodium lfide, hydrogen sulfide, or sodium hydrosulfide,

$$2R_2AsX + H_2S \longrightarrow (R_2As)_2S + 2HX.$$

2. By the action of hydrogen sulfide upon the corresponding arsine-ides,

$$(R_2As)_2O + H_2S \longrightarrow (R_2As)_2S + H_2O.$$

3. By treating arsinic acids with ammonium sulfide and subse-ıently acidifying, e. g.,

$$(O_2N.C_6H_4)_2AsO.ONH_4 + 8(NH_4)_2S \longrightarrow (H_2N.C_6H_4)_2AsS.SNH_4 + 6H_2O + 6S + 16NH_3$$

$$2(H_2N.C_6H_4)_2AsS.SNH_4 + 2HCl \longrightarrow [(H_2N.C_6H_4)_2As]_2S + 2NH_4Cl + H_2S + S_2.$$

4. From tetraaryldiarsines by combining with sulfur,

$$R_2As - AsR_2 + S \longrightarrow (R_2As)_2S.$$

With the exception of the oily phenyl-p-tolyl compound, they are ·nerally crystalline solids which are decomposed by concentrated haloid ·ids, yielding the corresponding monohalogenated arsines and hydrogen ılfide.

Diphenylarsinesulfide, $[(C_6H_5)_2As]_2S$.—Obtained by passing hydro-ɜn sulfide through an alcoholic solution of diphenylarsineoxide or ·hloroarsine;[775] also by treating the latter with either sodium sulfide[778] : sodium hydrosulfide.[779] It crystallizes from alcohol in colorless, silky ɜedles, m. p. 64-7°; easily soluble in benzene, chloroform or carbon isulfide, less so in alcohol, ether or glacial acetic acid and insoluble in lkalis or alkali monosulfides. With concentrated hydrochloric acid iphenylchloroarsine and hydrogen sulfide are obtained.

Phenyl-p-tolylarsinesulfide, $[C_6H_5(CH_3.C_6H_4)As]_2S$, is a viscid oil ·hich cannot be solidified.[780]

Di(3-nitrophenyl)arsinesulfide, $[(O_2N.C_6H_4)_2As]_2S$.—Warty aggre-ates of yellow needles, m. p. 156°; obtained by boiling an excess of ɜtra(3-nitrophenyl)diarsine with a benzene solution of sulfur.[781]

Di(3-aminophenyl)arsinesulfide, $[(H_2N.C_6H_4)_2As]_2S$.—Obtained by passing hydrogen sulfide through a strongly ammoniacal solution of di(3-nitrophenyl)arsinic acid, and subsequently acidifying with hydrochloric acid. After filtering and rendering ammoniacal, the sulfide separates as a white precipitate melting at 110° and forming soluble salts with acids. With bromine it forms bis(di- or tribromoaminophenyl)arsinic acid, depending upon the temperature. The sulfate, $[(H_2N.C_6H_4)As]_2S.2H_2SO_4$, crystallizes in snow-white leaflets.[781]

Di(3-acetylaminophenyl)arsinesulfide, $[(CH_3COHN.C_6H_4)_2As]_2S$, is prepared by acetylating the preceding compound. It melts at 175°, is readily soluble in alcohol and insoluble in ether.[744]

Tetraphenyldiarsinedisulfide, $[(C_6H_5)_2As]_2S_2$, is obtained from diphenylarsinic acid either by saturating its ammoniacal solution with hydrogen sulfide and acidifying with hydrochloric acid, or by treating its glacial acetic acid solution with hydrogen sulfide.[752] It crystallizes from alcohol in white leaflets sintering at 60°, melting at 110°, and dissolving readily in yellow ammonium sulfide with the probable formation of ammonium diphenylthioarsinate. Its behavior with organic solvents is similar to that of diphenylarsinesulfide.

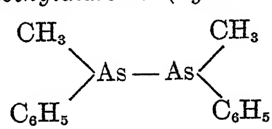
Tetra(3-nitrophenyl)diarsinetrisulfide, $[(O_2N.C_6H_4)_2As]_2S_3$, is a yellow powder, m. p. 69°; obtained by boiling a suspension of the tetra-(nitrophenyl)diarsine in benzene with an excess of sulfur.[752]

5. *Aromatic Cacodyls*, $R_2As-AsR_2$.—The derivatives of this group are less reactive than the corresponding members of the aliphatic series, and are chiefly prepared by reducing secondary aromatic arsineoxides or arsinic acids with phosphorous or hypophosphorous acid:

$$(R_2As)_2O + H_3PO_3 \longrightarrow R_2As-AsR_2 + H_3PO_4$$
$$2R_2AsO.OH + 3H_3PO_3 \longrightarrow R_2As-AsR_2 + 3H_3PO_4 + H_2O.$$

The products are generally crystalline substances either sparingly soluble or entirely insoluble in the usual organic solvents. They form the corresponding arsineoxides with oxygen, diarylarsinetrihalides with halogens, and arsonium compounds with alkyl halides under pressure in an atmosphere of carbon dioxide.

Symm. Diphenyldimethyldiarsine (Symm. Phenylmethylcacodyl),



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Upon refluxing an absolute alcoholic solution of phenylmethylarsineoxide with crystallized phosphorous acid, the diarsine separates as an oil which

;oon solidifies to crystals stable in air and melting at 70°. With methyl odide or bromide in a sealed tube filled with carbon dioxide it forms the :orresponding phenyltrimethylarsonium halide.[783]

Tetraphenyldiarsine (Phenylcacodyl), $(C_6H_5)_2As—As(C_6H_5)_2$, is)repared by refluxing alcoholic diphenylarsineoxide with an excess of)hosphorous acid;[511, 783] by heating alcoholic diphenylarsinic acid with ι large excess of the same reducing agent in a sealed tube for ten hours ιt 100°;[744] or by stirring diphenylchloroarsine with phosphorous acid ιt 100°.[778] It forms either a white, crystalline mass or elongated needles, n. p. 135°; slightly soluble in alcohol, less so in ether, and rapidly oxidiz-ng in air either to the anhydride of diphenylarsinic acid, $(C_6H_5)_4As_2O_3$, ır diphenylarsineoxide. With chlorine the diarsine forms diphenylar-inetrichloride; with methyl iodide in a sealed tube filled with carbon lioxide, diphenyldimethylarsonium iodide and diphenyliodoarsine are ›btained, while upon dry distillation it decomposes into triphenylarsine ınd free arsenic:

$$3(C_6H_5)_4As_2 \longrightarrow 4(C_6H_5)_3As + As_2.$$

'etra(3-nitrophenyl) diarsine, $(O_2NC_6H_4)_2As—As(C_6H_4NO_2)_2$, results ıpon reducing di(3-nitrophenyl)arsinic acid with a slight excess of phos-)horous acid in boiling glacial acetic acid, and separates in glistening eaflets melting at 200° and intumescing at higher temperatures. It is nsoluble in the ordinary solvents; combines readily with chlorine bro-nine or sulfur, and on boiling with a large excess of the latter in benzene nedium, is converted into tetra(3-nitrophenyl)diarsinetrisulfide.[784]

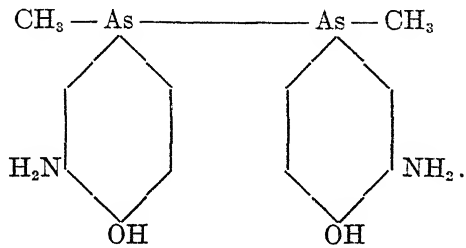
Tetra(3-aminophenyl) diarsine, $(H_2N.C_6H_4)_2As—As(C_6H_4.NH_2)_2$, s derived from the corresponding dinitroarsinic acid either by reduction vith tin and hydrochloric acid at 60°,[785] or with phosphorous acid in)oiling glacial acetic acid solution.[786] In the latter method the above liarsine is obtained as the acetate together with the corresponding tetra-ıcetyl derivative, separation being effected by pouring the cold reaction nixture into water, filtering off the insoluble yellow acetyl compound, ınd neutralizing the filtrate with dilute caustic soda, whereupon the 'ree diarsine separates as white flakes which readily turn gray. It can-ıot be obtained crystalline.

The *tetraacetyl derivative*,

$$(CH_3COHN.C_6H_4)_2As—As(C_6H_4.NHCOCH_3)_2,$$

s more stable than the corresponding amino compound, and can be pre-:ipitated from glacial acetic acid or alcoholic solution by the addition)f water, forming a white powder, m. p. 162°.[786]

Di(3-amino-4-hydroxyphenyl) dimethyldiarsine,

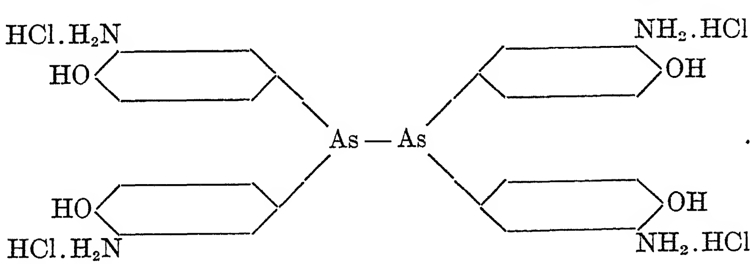


When 3-amino-4-hydroxyphenylmethylarsinic acid,

$$\begin{matrix} CH_3 \\ (H_2N)(OH)C_6H_3 \end{matrix} > AsO.OH$$

is treated with hypophosphorous acid (d, 1.136) containing a little hydriodic acid (d, 1.7), the diarsine separates as a hypophosphite which upon drying forms white crystals readily soluble in aqueous caustic alkalis or mineral acids, and insoluble in aqueous sodium carbonate. It yields a yellow diazo solution with sodium nitrate, reduces both Fehling's and Tollens' solutions, and intumesces violently when introduced into concentrated nitric acid. On shaking with methyl alcoholic hydrochloric acid, the hypophosphite is converted into the hydrochloride which may be precipitated by the addition of an excess of concentrated hydrochloric acid. It exists as a white crystalline powder readily soluble in water with a neutral reaction toward Congo paper. Both the hypophosphite and the hydrochloride are irritating to the mucous membrane.[787]

Tetra(3-amino-4-hydroxyphenyl) diarsine tetrahydrochloride,



Di(3-amino-4-hydroxyphenyl)arsinic acid is reduced like the preceding compound in an atmosphere of carbon dioxide at 60°, and the resulting solution introduced into hydrochloric acid. The white precipitate of the tetrahydrochloride is readily soluble in water or methyl alcohol.[758]

Symm. Diphenyldiiododiarsine, $\begin{array}{cc} C_6H_5As & - AsC_6H_5 \\ | & | \\ I & I \end{array}$. — Obtained

ither directly by the reduction of phenyldiiodoarsine with phosphorous .cid in alcoholic solution,[511] or by treating phenylarsineoxide with con- entrated hydriodic acid (d, 1.7), and then reducing in the same man- ıer.[443] It is an unstable compound crystallizing in bright yellow, leliquescent needles readily oxidizable in air to phenyldiiodoarsine and ɩhenylarsonic acid. With iodine it yields phenyldiiodoarsine, while with ııtric acid oxidation to phenylarsonic acid occurs with separation of ɔdine. When heated alone it decomposes into triphenylarsine, arsenic riiodide and free arsenic, but with methyl iodide at 100° it forms -iodophenyltrimethylarsonium iodide, and 4-iodophenyldiiodoarsine.[574] ıccording to Steinkopf,[788] however, the products obtained in the latter eaction are phenyltrimethylarsonium iodide and -triiodide, together vith phenyldiiodoarsine.

Symm. Di-m-xylyldiiododiarsine,

$$\begin{array}{cc} (CH_3)_2C_6H_3As & - AsC_6H_3(CH_3)_2, \\ | & | \\ I & I \end{array}$$

s a pale yellow, crystalline mass, m. p. 89°; obtained by adding iodine o an alcoholic suspension of arseno-m-xylene.[575]

Symm. Di-p-xylyldiiododiarsine is similarly prepared, and melts at 17°.[457]

Symm. Di(4-aminophenyl) dihydroxydiarsine,

$$\begin{array}{cc} H_2N.C_6H_4As & - AsC_6H_4.NH_2, \\ | & | \\ OH & OH \end{array}$$

onsisting of pale yellow flakes, m. p. 227°, is obtained as an intermediate product in the reduction of 4-aminophenylarsineoxide to the arseno com- ɔound by means of sodium amalgam in methyl alcoholic solution. It s soluble in dilute hydrochloric acid.[587]

C. Tertiary Derivatives.

1. *Tertiary Arsines,* R_3As.—In this chapter are included not only hose compounds containing three aromatic radicals attached to one ıtom of arsenic, but also those of the mixed type in which both aromatic ınd aliphatic groups are present. The latter are colorless, highly refrac- ive liquids which can be distilled undecomposed at reduced pressure ınd in some cases even at ordinary pressure in an atmosphere of carbon

dioxide. They have more or less unpleasant odors, are insoluble in water, generally soluble in alcohol, ether or benzene, and are mostly neutral in reaction, only a few of them exhibiting feebly basic properties. They combine additively with halogens, forming compounds of the type R_3AsX_2; yield arsonium compounds with alkyl halides; and form with alkyl- or aryldiiodoarsines addition products of the type $R_3As.R'AsI_2$. In benzene the latter are completely dissociated into their constituents, so that upon subsequent treatment with methyl iodide an arsonium iodide is precipitated while the alkyl- or aryldiiodoarsine remains in solution.

The mixed aliphatic-aromatic tertiary arsines are generally prepared:

1. From aryldihalogenated arsines and zinc dialkyls in ether medium:

$$RAsX_2 + ZnR'_2 \longrightarrow R'_2RAs + ZnX_2 \quad (X = \text{a halogen atom}).$$

2. By treating aryldihalogenated arsines with alkyl magnesium halides in ether or ligroin:

$$RAsX_2 + 2R'MgX \longrightarrow R'_2RAs + 2MgX_2.$$

3. From secondary monohalogenated arsines and the Grignard reagent in ether or benzene:

$$RR'AsX + R''MgX \longrightarrow RR'R''As + MgX_2.$$

4. By employing zinc dialkyls in ether instead of the Grignard reagent in the preceding method:

$$2RR'AsX + ZnR''_2 \longrightarrow 2RR'R''As + ZnX_2.$$

5. By condensing secondary halogenated arsines with an aromatic hydrocarbon in the presence of aluminium chloride.

On the other hand, the purely aromatic tertiary arsines are obtained:

1. By condensing aryl halides with arsenic trihalides by means of sodium in the presence of ether or xylene:

$$3RX + AsX_3 + 6Na \longrightarrow R_3As + 6NaX.$$

2. By employing aryl dihalogenated arsines instead of arsenic trihalides in the above reaction:

$$2RX + R'AsX_2 + 4Na \longrightarrow R_2R'As + 4NaX.$$

This method is especially suitable for preparing tertiary arsines with mixed aromatic radicals.

3. Upon treating arsenic trihalides or trioxide with the Grignard reagent:

$$3RMgX + AsX_3 \longrightarrow R_3As + 3MgX_2.$$

4. From primary aromatic arsineoxides by the action of heat:

$$3RAsO \longrightarrow R_3As + As_2O_3.$$

5. By reducing triaryl arsineoxides with phosphorous acid in alcohol, or with hydrogen sulfide or nascent hydrogen in glacial acetic acid:

$$R_3AsO - O \longrightarrow R_3As.$$

The products are crystalline solids insoluble in water, more or less soluble in various organic solvents, and, in contradistinction to the corresponding aliphatic compounds, possess no basic properties. Thus, they do not form salts with mineral acids unless one or more basic substituents are present in the nucleus, in which case the acid attaches itself to the basic radicals. In the same way it is possible to obtain alkaline salts, the metal replacing the hydrogen of a nuclear carboxyl or hydroxyl group. The arsines form double salts with mercuric, platinic or auric chloride; combine additively with halogens to the corresponding triarylarsine dihalides, with sulfur to the arsine sulfides and with alkyl halides to the arsonium compounds. With sulfur monochloride in an indifferent solvent such as dry ether or carbon bisulfide, they form addition products of the type $R_3As\begin{cases} Cl \\ S.S.Cl \end{cases}$, which are decomposed by water to the corresponding triarylarsine oxides:

$$R_3AsS_2Cl_2 + H_2O \longrightarrow R_3AsO + 2HCl + S_2.$$

Heating with arsenic trihalides converts the tertiary arsines into primary dihalogenated arsines:

$$R_3As + 2AsX_3 \longrightarrow 3RAsX_2.$$

Phenyldimethylarsine, $(C_6H_5)(CH_3)_2As$, may be obtained from phenyldichloroarsine by treatment with zinc dimethyl,[789] with methylmagnesium bromide in anhydrous ether,[790] or with methylmagnesium iodide in light petroleum.[734] Still more satisfactory results are obtained upon mixing dimethyliodoarsine, bromobenzene and magnesium in ether medium, allowing to stand at ordinary temperature for two hours, and adding ice and dilute hydrochloric acid. The ethereal layer which separates is dried over anhydrous sodium sulfate, the solvent removed by evaporation, and the residue distilled under diminished pressure,[791] when the arsine comes over as a colorless, refractive, moderately limpid liquid with an acute repulsive odor; b. p. 200°, 85°/14 mm.; soluble in alcohol or benzene but insoluble in water. With bromine it forms phenyldimethylarsine dibromide and with alkyl or aryl halides, arsonium salts. Addition products are also obtained with various inorganic iodides [792] or organic dihalogenated arsines,[793] forming compounds of the types $C_6H_5(CH_3)_2As.R'I$ and $C_6H_5(CH_3)_2As.RAsI_2$ respectively, where R′ represents an inorganic element and R either an alkyl or aryl radical.

$(C_6H_5)(CH_3)_2As.PI_3$, prepared from equimolar amounts of its constituents in carbon bisulfide medium, crystallizes in orange prisms melting at 140° and very difficult to purify owing to the readiness with which it absorbs water. $(C_6H_5)(CH_3)_2As.AsI_3$ consists of orange-red leaflets, m. p. 153°, and very sparingly soluble in the usual solvents.

$(C_6H_5)(CH_3)_2As.SbI_3$ crystallizes from benzene solution in orange prisms, m. p. 165°; sparingly soluble in the usual solvents.

$$(C_6H_5)(CH_3)_2As.BiI_3$$

separates from hot alcohol in very sparingly soluble vermilion prisms. m. p. 198-200°, while $2(C_6H_5)(CH_3)_2As.SnI_4$ forms chocolate-colored leaflets, m. p. 140-5°.

$(C_6H_5)(CH_3)_2As.CH_3AsI_2$, lemon-yellow needles from a mixture of acetone and ether, melts at 93-4°, and is completely dissociated into its constituents in benzene solution at concentrations up to five per cent. Methyl iodide in benzene solution converts it into phenyltrimethylarsonium iodide and methyldiiodoarsine. $(C_6H_5)(CH_3)_2As.C_2H_5AsI_2$ separates from alcohol in yellow crystals, m. p. 44°;

$$(C_6H_5)(CH_3)_2As.C_6H_5AsI_2$$

in orange prisms, m. p. 69°; and $(C_6H_5)(CH_3)_2As.C_6H_5AsCl$ in colorless needles, m. p. 36°.

4-Methylphenyldimethylarsine, $(CH_3.C_6H_4)(CH_3)_2As$, is obtained as a double zinc salt by the interaction of 4-methylphenyldichloroarsine and zinc dimethyl in ether medium. On decomposing with caustic soda the free arsine is liberated as a colorless liquid with an unpleasant odor; b. p. 220° in an atmosphere of carbon dioxide.[453]

α-Naphthyldimethylarsine, $(C_{10}H_7)(CH_3)_2As$, from dimethyliodoarsine and α-napthylmagnesium bromide, is a liquid boiling at 163-5°/13 mm. Its additive compound with methyldiiodoarsine crystallizes from alcohol in yellow needles, m. p. 76-7°.[794]

Phenyldiethylarsine is prepared from phenyldichloroarsine by treatment with zinc diethyl in benzene, ether [795] or light petroleum medium,[796] or better with methylmagnesium iodide in benzene solution.[793] It also results upon heating arsenobenzene and mercury diethyl in a sealed tube at 150°: [551]

$$C_6H_5As = AsC_6H_5 + 2Hg(C_2H_5)_2 2(C_6H_5)(C_2H_5)_2As + Hg.$$

The product is a colorless, highly refractive liquid with a faint unpleasant odor, b. p. 240°, 111-15°/14 mm., and is unaffected by concentrated hydrochloric acid. With halogens it combines additively to the corresponding arsinedihalides, with alkyl or aryl halides to arsonium compounds, and with alkyl dihalogenated arsines to compounds like those mentioned under phenyldimethylarsine. The product obtained with methyldiiodoarsine, $(C_6H_5)(C_2H_5)_2As.CH_3AsI_2$, crystallizes from alcohol or acetone in bright yellow needles, m. p. 78-9°.[797]

4-Methylphenyldiethylarsine, $(CH_3.C_6H_4)(C_2H_5)_2As$, prepared like the dimethyl compound by employing zinc diethyl, is a colorless, highly

refractive liquid with a faint, unpleasant odor; b. p. 250°; does not freeze at — 21°, and combines with alkyl iodides to form arsonium compounds.[798]

4-Carboxyphenyldiethylarsine [*Diethylarsinobenzoic acid*],

$$(HOOC.C_6H_4).(C_2H_5)_2As.$$

The corresponding arsine hydroxychloride is reduced in aqueous alcoholic solution with tin and hydrochloric acid, and the tin precipitated as the oxychloride by the addition of water, whereupon the arsine separates as a yellow oil. This is extracted with ether, the solvent evaporated off, and the oily residue dissolved in dilute ammonia, from which the free arsine is reprecipitated by hydrochloric acid. By recrystallization from dilute alcohol it is obtained as fine white needles, m. p. 58°; readily soluble in alcohol, ether or chloroform, insoluble in water or petroleum ether, and is reduced by nascent hydrogen to diethylarsine and benzoic acid. It possesses the properties of both a tertiary arsine and an acid, forming addition products with mercuric chloride, halogens, sulfur or methyl iodide, and yielding metallic salts. Of the latter only the alkali derivatives are soluble in water. The ammonium salt is a white crystalline mass, while the neutral barium and lead salts are white precipitates. The mercurichloride forms white silky leaflets, m. p. 171-2°; difficultly soluble in water.[799]

Phenylmethylethylarsine, $(C_6H_5)(CH_3)(C_2H_5)As$, results upon heating either phenylmethyliodoarsine [797] or the corresponding chloroarsine [800] with ethylmagnesium bromide in benzene solution. It is a colorless oil boiling at 97°/12-13 mm., and possessing chemical and physical properties intermediate between those of the corresponding dimethyl and diethyl derivatives.[797] Its addition product with methyldiiodoarsine crystallizes from alcohol in yellow needles melting at 84°, while that produced with phenyldiiodoarsine separates from alcohol in orange-yellow prisms melting at 55°.[794]

Phenylmethyl-n-propylarsine, $(C_6H_5)(CH_3)(C_3H_7)As$, from phenylmethylchloroarsine and n-propylmagnesium bromide, is a liquid, b. p. 105-6°/12 mm.[761]

Phenylmethyl-γ-phenylpropylarsine, $(C_6H_5)(CH_3)(C_6H_5.C_3H_6)As$, results from the interaction of phenylmethyliodoarsine and γ-phenylpropylmagnesium bromide in ethereal solution as a colorless, highly refractive liquid, b. p. 208°/17 mm. With methyl iodide it forms the corresponding arsonium compound.[801]

Phenylmethylallylarsine, $(C_6H_5)(CH_3)(C_3H_5)As$.—When magnesium powder is added to a mixture of molecular quantities of phenylmethylbromoarsine and allyl iodide in dry ether, a vigorous reaction occurs

with the formation of the above arsine together with a slight amount of diallyl. The purest product obtained thus far is a colorless liquid boiling at 192°, which cannot be further purified because it undergoes slight decomposition upon distillation and is too feebly basic to form stable salts.[802]

Phenylethyl-n-propylarsine, $(C_6H_5)(C_2H_5)(C_3H_7)As$, derived from phenylethylbromoarsine and zinc di-n-propyl in ethereal solution, is a colorless liquid with a characteristic odor, and boils at 245°. It has but feebly basic properties; is insoluble in concentrated hydrochloric acid, and oxidizes very slowly on exposure to air. With equimolar amounts of benzyl iodide at 40-50°, it combines to form phenylbenzylethyl-n-propylarsonium iodide.[803]

Diphenylmethylarsine, $(C_6H_5)_2(CH_3)As$, is prepared by the interaction of zinc dimethyl and diphenylchloroarsine in cold benzene solution in an atmosphere of carbon dioxide;[803] from phenylmagnesium bromide and methyldiiodoarsine,[794] or by gently heating phenylmethylchloroarsine with benzene in the presence of aluminium chloride.[219] The arsine is a colorless, highly refractive, oily liquid, b. p. 306°, 163-70°/15 mm.; readily soluble in alcohol or benzene and insoluble in water. It exhibits but a very slight tendency to form additive compounds.

Di(2-methylphenyl)methylarsine, $(C_7H_7)_2(CH_3)As$, is a pale yellow oil, b. p. 178-82°/12 mm.; solidifies on freezing and remelts at 42°/12 mm. It is prepared from methyldiiodoarsine and o-tolylmagnesium bromide.[805]

Phenylbenzylmethylarsine, $(C_6H_5)(C_7H_7)(CH_3)As$, from phenylmethylchloroarsine and benzylmagnesium bromide, boils at 174-7°/17 mm.[762]

Phenyl-α-napthylmethylarsine, $(C_6H_5)(C_{10}H_7)(CH_3)As$, from phenylmethyliodoarsine and α-naphthylmagnesium bromide, is a colorless, crystalline solid, m. p. 58°; b. p. 236-8°/17 mm.; readily soluble in ether. It is best crystallized from alcohol.[806]

Diphenylethylarsine, $(C_6H_5)_2(C_2H_5)As$, is a colorless liquid with a fruity odor; b. p. 320°, 162-3°/10 mm.; obtained from diphenylchloroarsine and zinc diethyl[807] or ethylmagnesium bromide.[808]

Phenyl-p-tolylethylarsine, $(C_6H_5)(C_7H_7)(C_2H_5)As$, from zinc diethyl and phenyl-p-tolylchloroarsine, is a colorless oil with a fruity odor, boiling at 210-25°/50 mm.[809]

Triphenylarsine, $(C_6H_5)_3As$, has been the subject of many investigations, and various methods have been developed for its preparation.

Very satisfactory results have been obtained from the interaction of phenylmagnesium bromide and either arsenic trichloride,[810, 742] tri-iodide,[811] or trioxide.[812] An equally satisfactory method consists in condensing phenyl chloride or bromide with arsenic trichloride by means of sodium in an ethereal [813, 442] or xylene medium.[814] It may also be obtained by heating triphenylarsine oxide at 180°; [815] from triphenylstibine and finely powdered arsenic in a sealed tube at 350° for eight hours: [816]

$$4(C_6H_5)_3Sb + As_4 \longrightarrow 4(C_6H_5)_3As + Sb_4;$$

by heating symm. diphenyldiododiarsine: [511]

$$3(C_6H_5)_2As_2I_2 \longrightarrow 2(C_6H_5)_3As + 2AsI_3 + As_2;$$

and as a by-product in the preparation of diphenylchloroarsine from phenyldichloroarsine and mercury diphenyl.[817]

The compound crystallizes from alcohol in colorless, vitreous, transparent, triclinic plates, d, 1.306; m. p. 58-60°; and boiling undecomposed above 360° in an atmosphere of carbon dioxide. It is readily soluble in ether, benzene or hot alcohol, difficultly in cold alcohol and insoluble in water, hydrochloric or hydriodic acids. It dissolves in ethyl iodide but does not form an arsonium compound even at 100°; by prolonged heating with arsenic trichloride in a sealed tube at 250°, phenyldichloroarsine is obtained, while with phosphorus at 300° for four hours the corresponding phosphine is formed:

$$4(C_6H_5)_3As + P_4 \longrightarrow 4(C_6H_5)_3P + As_4.$$

The arsine combines additively with halogens, sulfur, methyl iodide, chloroacetic acid, metallic salts and sulfur monochloride. The mercurichloride, obtained from its components in alcoholic medium, separates from dilute solutions as nacreous leaflets, and from concentrated solutions as white, pulverulent crystals easily soluble in hot absolute alcohol, less so in dilute and practically insoluble in water. It is unaffected by cold aqueous potassium hydroxide, but upon boiling yields triphenylarsine dihydroxide, potassium chloride and mercury. The arsine may be liberated from its mercurichloride by treatment with cold alcoholic potash, or by passing hydrogen sulfide into its alcoholic solution:

$$(C_6H_5)_3As.HgCl_2 + 2KOH \longrightarrow (C_6H_5)_3As + HgO + 2KCl + H_2O$$
$$(C_6H_5)_3As.HgCl_2 + H_2S \longrightarrow (C_6H_5)_3As + HgS + 2HCl.$$

This ability of triphenylarsine to combine with mercuric chloride can be utilized in separating it from diphenylchloroarsine which forms no such addition product.[818] The platinichloride crystallizes from alcohol or chloroform in pale-yellow leaflets, m. p. 285°.[819]

The sulfur monochloride addition product, $(C_6H_5)_3As\left<\begin{array}{l}Cl\\ S-S-Cl\end{array}\right.$, prepared by refluxing a dry ethereal solution of its constituents with the exclusion of atmospheric moisture, is a yellowish-white, crystalline precipitate which cannot be purified on account of its instability. It melts at 200°; is readily soluble in carbon bisulfide, chloroform or alcohol, difficultly so in petroleum ether or benzene, insoluble in ether and easily soluble in water with the separation of sulfur. When boiled with aqueous ammonia it is converted into triphenylarsine dihydroxide.[820]

Tri(2-methylphenyl)arsine, $(C_6H_4.CH_3)_3As$, from o-tolylmagnesium bromide and arsenic triiodide, crystallizes from alcohol in colorless needles melting at 98°.[811]

Tri(3-methylphenyl)arsine is prepared from m-bromo-toluene, arsenic trichloride and sodium in anhydrous ether. It separates from alcohol as white leaflets, from ether as prismatic and tabular crystals of the rhombic system, m. p. 96°; d, 1.31/18°; readily soluble in ether, alcohol, benzene or glacial acetic acid and sparingly so in ligroin. It readily forms arsonium compounds with alkyl iodides. The mercurichloride, m. p. 174°, is fairly soluble in glacial acetic acid but only sparingly in alcohol.[821]

Tri(4-methylphenyl)arsine.—The most convenient method of preparation consists in adding sodium shavings or wire to a solution of 4-bromotoluene and arsenic trichloride in anhydrous ether.[824] It may also be obtained from p-tolylmagnesium bromide and arsenic trioxide in ethereal solution,[774] or by heating p-tolylarsine in a sealed tube at 360°,[825] forming large colorless crystals, m. p. 145°; b. p. above 360° without decomposition; readily soluble in ether, chloroform, carbon bisulfide, glacial acetic acid or benzene, but less so in alcohol. Its mercurichloride is a white crystalline powder, m. p. 246°; soluble in hot glacial acetic acid.

Tri(4-ethylphenyl)arsine, $(C_2H_5.C_6H_4)_3As$, from 4-bromoethylbenzene, arsenic trichloride and metallic sodium, is a crystalline solid, m. p. 78°; readily soluble in ether, but sparingly in alcohol. Its mercurichloride melts at 132°.[828]

Tribenzylarsine, $(C_6H_5.CH_2)_3As$, results upon refluxing for 5-6 hours a mixture of arsenic trichloride and benzyl chloride (2 moles) in dry ether, to which sodium shavings (5 moles) and a small amount of pure ethyl acetate have been added. After cooling, another small quantity of ethyl acetate is added and the reaction permitted to continue for

12-14 hours longer, when the greater part of the arsine crystallizes out. The filtrate contains the remaining fraction of the arsine together with dibenzylarsinetrichloride and tribenzylarsine dichloride.

The arsine crystallizes from alcohol in colorless, transparent, monoclinic prisms, m. p. 104°; easily soluble in ether, benzene or glacial acetic acid, sparingly in cold alcohol and insoluble in water. It combines additively with halogens, sulfur or alkyl iodides; is oxidized by hot dilute nitric acid to benzoic and arsenic acids, but is unaffected by hydrochloric acid, even upon boiling in concentrated solution.[826] The mercurichloride crystallizes from alcohol in white needles, m. p. 159°, which upon boiling with aqueous or, better, alcoholic caustic potash is decomposed into the arsine and mercuric oxide, while with hydrogen sulfide the free arsine together with a slight amount of tribenzylarsine sulfide is obtained.[827]

Diphenyl-4-methylphenylarsine, $(C_6H_5)_2(C_6H_4.CH_3)As$, results upon warming p-tolyldichloroarsine, bromobenzene (2 moles) and thinly sliced sodium in anhydrous ether for about three days. It may be obtained in small, transparent crystals melting at 50°, by maintaining its alcoholic solution at low temperatures for weeks. The mercurichloride crystallizes from hot glacial acetic acid and melts at 147°, while the platinichloride is a yellow precipitate, m. p. 233°.[822]

Phenyldi(4-methylphenyl)arsine, $(C_6H_5)(C_6H_4.CH_3)_2As$, results from the interaction of phenyldichloroarsine, 4-bromotoluene (2 moles) and finely divided sodium in dry ether, the temperature of the reaction being regulated by external cooling. It crystallizes from hot alcohol in well-defined, white rhombohedra, m. p. 101°; easily soluble in ether, chloroform, benzene or hot alcohol and sparingly in cold alcohol or glacial acetic acid. Its mercurichloride forms white crystals melting at 210° and soluble in hot alcohol, while the platinichloride,

$$[C_6H_5(C_7H_7)_2As]_2.H_2PtCl_6,$$

consists of yellow crystals, m. p. 256°.[823]

Phenyldi(2,4-dimethylphenyl)arsine, $(C_6H_5)[C_6H_3(CH_3)_2]_2As$, is similarly prepared from 4-bromo-m-xylene. It separates from alcohol-ether in highly refractive, triclinic crystals, m. p. 99°; readily soluble in most organic solvents but sparingly in cold alcohol. The mercurichloride separates from alcohol-chloroform as lustrous needles, m. p. 224°; the platinichloride crystallizes from alcohol in yellow felted needles melting above 300° with decomposition.[829]

Tri(2,4-dimethylphenyl)arsine, $[C_6H_3(CH_3)_2]_3As$, is quantitatively obtained by the interaction of bromo-m-xylene, arsenic trichloride and sodium in dry ether at ordinary temperature. Recrystallized from alcohol-petroleum, it forms lustrous, transparent prisms, m. p. 166°;

easily soluble in ether, benzene or petroleum ether, but only sparingly in alcohol. Its mercurichloride melts at 257°.[830]

Tri(2,5-dimethylphenyl)arsine, prepared like the preceding isomeride from bromo-p-xylene, crystallizes from a mixture of alcohol, petroleum ether and benzene in lustrous, white prisms, m. p. 157°; readily soluble in ether, chloroform or benzene, sparingly in alcohol or petroleum ether. The mercurichloride melts at 236°.[831]

Phenyldi(2,4,5-trimethylphenyl)arsine, $(C_6H_5)[C_6H_2(CH_3)_3]_2As$, from phenyldichloroarsine, bromopseudocumene and sodium, melts at 138.5°; is readily soluble in most organic solvents but only sparingly in cold alcohol. Upon oxidation with potassium permanganate in alkaline solution no uniform acids are produced; this is attained only by heating with nitric acid in sealed tubes. The mercurichloride crystallizes from hot glacial acetic acid as silvery leaflets, m. p. 233°; easily soluble in chloroform and sparingly so in alcohol or glacial acetic acid; the platinichloride forms yellow rosets, m. p. 287°; readily soluble in chloroform; the aurichloride, $C_6H_5(C_9H_{11})_2As.HAuCl_4$, consists of colorless aggregates melting at 177° to a golden yellow mass.[832]

Tri(2,4,5-trimethylphenyl)arsine, $[C_6H_2(CH_3)_3]_3As$, is obtained like the xylyl compounds from bromopseudocumene, the reaction being completed by prolonged warming on a water-bath. It crystallizes in snow-white needles, m. p. 223°; easily soluble in warm benzene, sparingly in alcohol or petroleum ether and practically insoluble in ether.[833]

Tri(2,4,6-trimethylphenyl)arsine, similarly prepared from bromomesitylene by heating in a reflux apparatus for several days, forms tufts of prisms from hot alcohol, m. p. 170°; readily soluble in ether, chloroform, or petroleum ether and sparingly in alcohol or glacial acetic acid.[834]

Tri(4-isopropylphenyl)arsine, $[C_6H_4.CH(CH_3)_2]_3As$, from 4-bromocumene at ordinary temperature, separates from ether-alcohol as colorless prisms, m. p. 139-40°; readily soluble in ether, chloroform or hot alcohol. The mercurichloride consists of white needles, m. p. 243°.[835]

Tri(tertiary-butylphenyl)arsine, $[C_6H_4.C(CH_3)_3]_3As$.—Tertiary-butylbromobenzene in benzene solution is refluxed with arsenic trichloride and metallic sodium, the filtrate concentrated to incipient crystallization, and the arsine completely precipitated by the addition of alcohol. It forms white crystals, m. p. 235°; readily soluble in benzene, chloroform or carbon tetrachloride and sparingly in alcohol or ether.[836]

Tri-α-naphthylarsine, $(C_{10}H_7)_3As$.—To a dry ethereal solution of α-bromonaphthalene are added arsenic trichloride and metallic sodium,

the whole permitted to react at ordinary temperature in a reflux apparatus for 24 hours, and then warmed on a water-bath for 15-20 hours. When the reaction is completed the product is filtered, the residue extracted with ether, and the latter evaporated from the combined filtrate and extract. From the remaining dark brown, oily mass admixed tarry products are removed by means of ether, and the residual crude arsine purified by dissolving in hot benzene and reprecipitating with an equal volume of alcohol.[837] More satisfactory yields are obtained by warming α-naphthylmagnesium bromide and arsenic trichloride in absolute ether for two hours on a water-bath, and subsequently decomposing with ice and dilute hydrochloric acid.[742, 838]

The arsine crystallizes from benzene-alcohol in prisms, from benzene in rhombic plates, m. p. 250-2°; readily soluble in carbon bisulfide or hot benzene, sparingly in alcohol, ether, chloroform or cold benzene and insoluble in petroleum ether. Unlike its β-isomer, it forms no mercurichloride. By warming with sulfur monochloride in carbon bisulfide solution, it forms a crystalline addition product, m. p. 175° with decomposition; readily soluble in warm alcohol or chloroform and difficultly so in ether, carbon bisulfide or benzene.

Tri-β-naphthylarsine is prepared like its α-isomer from β-bromonaphthalene. After distilling off the ether from the filtrate, the residue is extracted successively with alcohol and petroleum ether to remove any naphthalene and tarry impurities, and the remaining crude arsine purified through its mercurichloride. The latter, after recrystallization from hot glacial acetic acid, is decomposed by hydrogen sulfide to the free arsine and mercuric sulfide.

The product forms colorless crystals, m. p. 165°; readily soluble in benzene, carbon bisulfide or chloroform and sparingly in ether or hot glacial acetic acid. The mercurichloride forms leaflets, m. p. 247°.[839]

Tri(4-phenylphenyl)arsine, $(C_6H_5.C_6H_4)_3As$, m. p. 183°, is obtained from 4-bromodiphenyl, arsenic trichloride and metallic sodium in ether.[840]

Tri(3-nitrophenyl)arsine, $(O_2N.C_6H_4)_3As$, produced by warming the corresponding arsineoxide with crystallized phosphorous acid in alcohol, is a yellow, crystalline powder, m. p. 250°; soluble in alcohol.[841]

Tri(?-chloro-3-nitrophenyl)arsine, $(O_2N.C_6H_3Cl)_3As$, similarly prepared from the corresponding arsineoxide, is a white powder, m. p. 252°; readily soluble in alcohol, chloroform or glacial acetic acid.[842]

Tri(3-nitro-4-methylphenyl)arsine, $(O_2N.C_6H_3.CH_3)_3As$, is made like the previous two compounds from the arsineoxide. It crystallizes from alcohol in white needles, m. p. 201°; easily soluble in chloroform or hot alcohol.[842]

3,3'-Dinitro-3''-aminotriphenylarsine, $(O_2N.C_6H_4)_2(H_2N.C_6H_4)As$, is a grayish-white solid, m. p. 205°, obtained by passing hydrogen sulfide through a glacial acetic acid solution of tri(3-nitrophenyl)arsine oxide.[843]

Tri(3-aminophenyl)arsine, $(H_2N.C_6H_4)_3As$, results upon reducing a glacial acetic acid solution of tri(3-nitrophenyl)arsine oxide with tin and concentrated hydrochloric acid. When the reaction is completed, the entire mixture is poured into water, an excess of concentrated aqueous caustic soda added, and the resulting curdy, white precipitate of the crude aminoarsine filtered off, dissolved in dilute hydrochloric acid, and treated with hydrogen sulfide to precipitate the last traces of tin. After neutralizing the filtrate, the resulting precipitate is further purified by dissolving in hot alcohol, concentrating and reprecipitating with water when a colorless, crystalline mass, m. p. 176°, is obtained.[844] Michaelis, however, isolated the same compound by reducing the nitro arsineoxide as above, diluting with hydrogen sulfide water, and precipitating the last traces of tin with hydrogen sulfide. Upon neutralization with caustic soda, he obtained a white precipitate which rapidly turned gray in the air.[845]

The arsine is soluble in alcohol, insoluble in water, and forms soluble salts with dilute mineral acids. The trihydrochloride,

$$[(HCl.H_2N)C_6H_4]_3As,$$

consists of pale red crystals and forms a yellow platinichloride, $[(HCl.H_2NC_6H_4)_3As]_2(PtCl_4)_3$, insoluble in cold but slightly soluble in hot water. The sulfate, $[(H_2N.C_6H_4)_3As]_2.3H_2SO_4$, is a stable substance readily soluble in dilute hydrochloric acid but sparingly so in cold water.

Tri(4-aminophenyl)arsine.—A dilute hydrochloric acid solution of 4-aminophenylarsineoxide is boiled for a very short time, and after standing for several hours is poured into an excess of ice-cold caustic soda solution. The arsine then separates as snow-white flakes which crystallize from alcohol-water in lustrous, quadrangular plates, m. p. 173-4°. The reaction, although not quantitative, is expressed by the equation:

$$3H_2N.C_6H_4AsO \longrightarrow (H_2N.C_6H_4)_3As + As_2O_3.$$

The compound is easily soluble in acetone, pyridine, ethyl acetate or glacial acetic acid, less so in methyl or ethyl alcohol, sparingly in benzene or chloroform and insoluble in water, ligroin or aqueous caustic soda. It dissolves in dilute mineral acids with the formation of crystalline salts.[846]

Tri(3-amino-4-methylphenyl)arsine, $(H_2N.C_6H_4.CH_3)_3As$, is prepared from the corresponding trinitro arsine or trinitro arsine oxide by

reducing with tin and hydrochloric acid. It crystallizes from hot alcohol in stable, white prisms, m. p. 198°; soluble in dilute acids and sparingly in cold alcohol, ether or water. The hydrochloride is precipitated by concentrated hydrochloric acid and forms fine white needles; the sulfate $[(H_2N.C_6H_3.CH_3)_3As]_2.3H_2SO_4$, is a crystalline precipitate sparingly soluble in hot dilute hydrochloric acid and almost insoluble in water.[847]

Tri(3-acetylaminophenyl)arsine, $(CH_3COHN.C_6H_4)_3As$, crystallizes in colorless needles, m. p. 230° (Philips), 233° (Michaelis); easily soluble in glacial acetic acid and sparingly in alcohol. It is prepared by warming the corresponding amino compound with acetic anhydride.[848]

Tri(4-acetylaminophenyl)arsine crystallizes with one molecule of water when prepared by boiling the amino compound with acetic anhydride for one minute, then with methyl alcohol for five minutes, and finally precipitating by the gradual addition of water. It forms warty aggregates of small, white needles which lose their water of crystallization at 110°, melt at 170-1°, and upon further heating resolidify and finally remelt at 232-3°.

An anhydrous variety may be obtained by treating the amino compound with acetic anhydride as above and allowing to stand for 24 hours. It crystallizes from absolute alcohol in warty aggregates of transparent prisms, m. p. 243°. Both modifications are soluble in glacial acetic acid, methyl or ethyl alcohol and insoluble in water, ether, benzene or dilute mineral acids. The arsine is oxidized to the corresponding arsine oxide by iodine in aqueous acetic acid solution containing sodium acetate.[849]

Tri(3-acetylamino-4-methylphenyl)arsine,

$$(CH_3COHN.C_6H_3.CH_3)_3As,$$

obtained by dissolving the corresponding amino compound in acetic anhydride, melts at 228°.[850]

Tri(3-benzoylaminophenyl)arsine, $(C_6H_5COHN.C_6H_4)_3As$, is a crystalline powder melting at 271°, insoluble in all ordinary solvents, and results upon warming the amino compound with benzoyl chloride.[851]

Tri(3-benzylamino-4-methylphenyl)arsine,

$$(C_6H_5CH_2HN.C_6H_3.CH_3)_3As,$$

is obtained as a hydrochloride by warming the amino arsine with benzyl chloride.[852]

Tri(4-dimethylaminophenyl)arsine, $[(CH_3)_2N.C_6H_4]_3As$, is precipitated as a white, caseous mass upon mixing dimethylaniline and arsenic trichloride at ordinary temperature, stirring the resulting syrupy mass

into water, and treating the filtrate with an excess of concentrated caustic soda. The arsine is purified by removing the excess of dimethylaniline with steam, dissolving the residual product in chloroform and reprecipitating with alcohol.[853, 854] It separates from hot alcohol in long, white needles, m. p. 240°; readily soluble in dilute acids, from which it is reprecipitated unchanged by alkalis. When boiled with sulfur monochloride in carbon bisulfide solution, it forms a crystalline addition product, m. p. 137-41°; readily soluble in chloroform, difficultly so in carbon bisulfide or ether, and decomposing in dilute hydrochloric acid with the separation of sulfur and the simultaneous formation of tri(4-dimethylaminophenyl)arsine oxide. With 2-nitrophenylsulfur monochloride in benzene solution the arsine combines additively, forming the compound, $[(CH_3)_2N.C_6H_4]_3As\begin{cases} Cl \\ S-C_6H_4.NO_2 \end{cases}$, which melts with decomposition at 201°, is easily soluble in carbon bisulfide or chloroform, difficultly so in benzene, ether or alcohol, and is decomposed by water into the corresponding tertiary arsineoxide and di(2-nitrophenyl)disulfide, $(O_2N.C_6H_4)_2S_2$.[855]

Tri(4-methoxyphenyl)arsine, $(CH_3O.C_6H_4)_3As$.—Upon adding a slight amount of ethyl acetate to a mixture of 4-bromoanisole, an excess of arsenic trichloride and finely sliced sodium in ether, a vigorous reaction ensues, and the greater part of the arsine formed separates out along with sodium chloride, some unattacked sodium and metallic arsenic. The sodium is first removed by means of water, and the dried residue extracted with hot benzene from which, after concentration, the arsine separates in hard crystals which can be further purified from a mixture of benzene and alcohol. The product forms colorless, transparent, cubical crystals, m. p. 156°; easily soluble in benzene, difficultly so in alcohol or ether, and combines with halogens less readily than triphenylarsine. It is completely converted into arsenic acid when heated with bromine and water at 150°.[856] Heating with hydriodic acid at higher temperatures decomposes it into p-anisole and arsenic triiodide.[756]

Tri(4-ethoxyphenyl)arsine, $(C_2H_5O.C_6H_4)_3As$, m. p. 88-9°, is obtained in very poor yield from 4-bromophenetole like the preceding compound, but on account of its great solubility in ether, is isolated by evaporating off the latter, extracting the residue with absolute alcohol and removing the solvent.[857]

Tri(4-carboxyphenyl)arsine [Tri-p-benzarsenious acid, Arsinotribenzoic acid], $(HOOC.C_6H_4)_3As$, which results upon reducing the corre-

sponding arsine dihydroxide with hydriodic acid and red phosphorus, crystallizes from ether in colorless needles melting with decomposition at high temperatures. Its sodium salt, $(NaOOC.C_6H_4)_3As.2H_2O$, obtained but once, separated from hot water as colorless needles, while the silver salt, $(AgOOC.C_6H_4)_3As$, is a pale yellow precipitate.[858]

Chapter V. Pentavalent Aromatic Arsenicals.

A. Primary Derivatives.

1. *Aryl Arsinetetrahalides and -Oxyhalides,* $RAsX_4$, $RAsOX_2$.—The aromatic arsinetetrahalides, which are more stable than the corresponding aliphatic compounds, may be readily obtained by the addition of halogens to the corresponding dihalogenated arsines:

$$RAsX_2 + X_2 \longrightarrow RAsX_4.$$

In the case of 3-nitrophenylarsinetetrachloride, however, the starting material is the corresponding nitro arseno compound:

$$O_2N.C_6H_4As = AsC_6H_4.NO_2 + 4Cl_2 \longrightarrow 2O_2N.C_6H_4AsCl_4,$$

while the hydriodide of 4-aminophenylarsinetetraiodide results upon reducing the amino arsonic acid with hydriodic acid:

$$H_2N.C_6H_4AsO(OH)_2 + 5HI \longrightarrow (HI.H_2N)C_6H_4AsI_4 + 3H_2O.$$

The products are generally crystalline compounds with the exception of 2-methylphenylarsinetetrachloride which is a viscous liquid, and the corresponding 4-methylphenyl compound which is a semi-solid mass at ordinary temperature. They are readily decomposed by water to the corresponding arsonic acids with the intermediate formation of the oxyhalides:

$$\begin{cases} RAsX_4 + H_2O \longrightarrow RAsOX_2 + 2HX \\ RAsOX_2 + 2H_2O \longrightarrow RAsO(OH)_2 + 2HX. \end{cases}$$

When heated they decompose into aryl halides and arsenic trihalides:

$$RAsX_4 \longrightarrow RX + AsX_3.$$

With an excess of bromine the arsenic radical is split off, yielding a dibromobenzene derivative.

The oxyhalides are crystalline compounds formed upon the direct addition of halogens to arylarsineoxides:

$$RAsO + X_2 \longrightarrow RAsOX_2.$$

They are also readily decomposed by water to the corresponding arsonic acids, and by heat to an aryl halide and arsenious oxychloride:

$$RAsOX_2 \longrightarrow RX + AsOX.$$

In addition, this chapter includes several esters of phenylarsineoxychloride, $C_6H_5As(OR')Cl_2$, prepared by the action of chlorine upon the corresponding esters of phenylarsenious acid (phenyldialkoxyarsines):

$$C_6H_5As(OR')_2 + Cl_2 \longrightarrow C_6H_5As(OR')_2Cl_2.$$

These are crystalline compounds readily hydrolyzed by water to phenylarsonic acid:

$$C_6H_5As(OR')_2Cl_2 + 3H_2O \longrightarrow C_6H_5AsO(OH)_2 + 2R'OH + 2HCl.$$

Phenylarsinetetrachloride, $C_6H_5AsCl_4$, prepared by saturating phenyldichloroarsine with chlorine, consists of broad, yellow needles fuming in air and melting at 45°. In its violent decomposition by water it resembles the corresponding phosphorus compound, but, unlike the latter, it acts as a chlorinating agent with organic acids, replacing a hydrogen atom by a chlorine, while the phosphorus compound replaces a hydroxyl group by a chlorine atom. Thus, when phenylarsinetetrachloride is warmed with acetic acid, chloroacetic acid is formed:

$$C_6H_5AsCl_4 + CH_3COOH \longrightarrow CH_2Cl.COOH + HCl + C_6H_5AsCl_2.$$

On heating the arsinetetrachloride in an open vessel, it dissociates into the corresponding dichloroarsine and chlorine, but heating in a sealed tube at 150° decomposes it into phenyl chloride and arsenic trichloride. It does not react with one mole of bromine, but is decomposed by an excess, yielding p-dibromobenzene.[859]

2-Methylphenylarsinetetrachloride, $CH_3.C_6H_4AsCl_4$, similarly prepared, is a dark yellow, viscous liquid which upon treatment with water yields the corresponding arsonic acid.[860]

3-Methylphenylarsinetetrachloride is a crystalline solid melting at 38°.[509]

4-Methylphenylarsinetetrachloride is a yellow, semi-solid mass at ordinary temperature, but solidifies upon cooling.[860]

2,4-Dimethylphenylarsinetetrachloride, $(CH_3)_2C_6H_3AsCl_4$, is a white crystalline mass.[861]

4-Phenylphenylarsinetetrachloride, $(C_6H_5)C_6H_4AsCl_4$, has also been prepared.[555]

3-Nitrophenylarsinetetrachloride, $O_2N.C_6H_4AsCl_4$, is derived from 3,3′-dinitroarsenobenzene by suspending in chloroform and introducing chlorine. It forms long needles readily absorbing moisture from the air with the formation of the corresponding arsonic acid.[516]

4-Aminophenylarsinetetraiodide hydriodide, $(HI.H_2N)C_6H_4AsI_4$, is made by warming the corresponding arsonic acid with hydriodic acid (d, 1.7). It crystallizes from hot glacial acetic acid in orange-red crystals, m. p. 140°; insoluble in the usual organic solvents, and yielding the corresponding arsineoxide with water.[862]

Phenylarsineoxychloride, $C_6H_5AsO.Cl_2$, may be obtained by regulating the action of water upon the arsinetetrachloride. A more satisfactory method, however, consists in permitting chlorine to interact with phenylarsineoxide. It is a white, crystalline substance fuming in air, melting at about 100°, and readily dissolving in water with the formation of phenylarsonic acid. Heated in a sealed tube at 120° for several hours, it decomposes into chlorobenzene and arsenious oxychloride.[863]

Phenyldimethoxyarsine dichloride, $C_6H_5As(OCH_3)_2Cl_2$, from phenyldimethoxyarsine and chlorine, forms colorless crystals melting at 90°, and hydrolyzed by either water or alcohol to phenylarsonic acid, methyl alcohol and hydrochloric acid. The diethyl ester consists of cubical crystals melting at 95°.[864]

Phenylarsineoxybromide is obtained together with bromobenzene by the action of bromine upon phenylarsineoxide.[865]

2-Methylphenylarsineoxychloride is derived from the arsineoxide and chlorine.[866]

4-Methylphenylarsineoxychloride melts at 69°, but decomposes into 4-chlorotoluene and arsenious oxychloride when heated in a sealed tube above 200°.[866] The corresponding *arsineoxybromide* has also been prepared.[867]

2,4-Dimethylphenylarsineoxychloride melts at 150°,[510] and its *2,5-isomer* at 178°.[457]

2. *Aryl Arsonic Acids.* $RAsO(OH)_2$. Despite the fact that Rosemund [868] recently succeeded in obtaining a slight amount of phenylarsonic acid by heating bromobenzene with aqueous tripotassium arsenite and a little copper sulfate in a sealed tube at 180-200° for six hours, it can be safely stated that no method has as yet been devised by which aromatic hydrocarbons may be directly arsenated. In 1910, however, Bart [86] patented a very satisfactory and efficient method of preparing aryl arsonic acids which consists in diazotizing arylamines and treating the resulting diazo, or better isodiazo, compounds with sodium arsenite in either alkaline or neutral solution, the reaction proceeding according to the equation:

$$RN = NX + Na_3AsO_3 \longrightarrow RAsO(ONa)_2 + NaX + N_2.$$

In the preparation of phenylarsonic acid by this method, the yields obtained with the normal diazobenzene compound are very small, but with potassium benzeneisodiazo oxide the results are more satisfactory. If, however, the starting materials are nuclear substituted arylamines, the reactivity of the corresponding normal diazo compound is increased to such an extent that conversion into the arsonic acid proceeds very readily without the necessity of first preparing the isodiazo compound. This procedure is not only suited for the preparation of primary arsonic acids, but also of diarylarsinic acids and triarylarsine oxides:

$$RN = NX + RAs(ONa)_2 \longrightarrow R_2AsO.ONa + NaX + N_2$$
$$RN = NX + R_2AsONa \longrightarrow R_3AsO + NaX + N_2.$$

Later it was noted that the reaction with normal diazo compounds could be facilitated by the use of catalysts such as metallic copper, cuprous hydroxide or other copper salts in the absence of free alkali.[87] In 1912 Bart further improved his original method by employing as catalysts metallic copper, silver, nickel, cobalt or their salts in alkaline solution, thereby facilitating the removal of the diazo-nitrogen at low temperatures, and at the same time obviating the formation of by-products.[88]

According to H. Schmidt, however, a neutral or slightly acid medium is most suitable for the interaction of normal diazo compounds and potassium arsenite without the assistance of any catalyst. In this procedure various arsenated as well as non-arsenated by-products are obtained. Thus, in the preparation of phenylarsonic acid there is also obtained 4-phenylphenylarsonic acid, while the products derived from 3-nitrodiazobenzene are the corresponding nitroarsonic acid and 4?-(3′-nitrophenyl)-3-nitrophenylarsonic acid.[90]

In 1919 Mouneyrat modified Bart's process so that arsonic acids could be prepared by causing normal diazo compounds to act upon cold or warm aqueous or dilute alcoholic solutions of arsenious acid in an acid, neutral or alkaline medium, in the presence of special catalyzers. The characteristic feature of this process consists in the simultaneous use of two catalysts, one a copper salt, and the other a reducing agent the nature of which varies according to the acidity or alkalinity of the medium. If an acid medium is employed, an acid reducing agent such as hypophosphorous acid, cuprous hydrate, etc., must be used; in a neutral medium, sodium hydrosulfite or sodium formaldehydesulfoxylate may be employed, while in an alkaline solution, the latter two reducing agents or an excess of alkali arsenite are satisfactory.[89]

The arylarsonic acids may also be obtained:

1. From aminoarylarsonic acids by diazotizing and replacing the diazo group with a hydrogen atom in the usual manner.

2. By oxidizing arylarsines, e. g., with nitric acid:

$$RAsH_2 + 3O \longrightarrow RAsO(OH)_2.$$

3. From dichloroarsine by chlorinating in the presence of water, or by oxidizing with hydrogen peroxide in glacial acetic acid solution:

$$RAsCl_2 + Cl_2 \longrightarrow RAsCl_4 \xrightarrow{3H_2O} RAsO(OH)_2 + 4HCl$$
$$RAsCl_2 + H_2O_2 + H_2O \longrightarrow RAsO(OH)_2 + 2HCl.$$

4. Upon oxidizing arsineoxides, e. g., with hydrogen peroxide in alkaline solution:

$$RAsO + O + H_2O \longrightarrow RAsO(OH)_2.$$

5. By oxidizing arseno compounds, e. g., with iodine:

$$\left| \begin{array}{l} RAs = AsR + 2I_2 + 2H_2O \longrightarrow 2RAsO + 4HI \\ 2RAsO + I_2 + 2H_2O \longrightarrow 2RAsO(OH)_2 + 2HI. \end{array} \right.$$

6. By hydrolyzing arsinetetrahalides or -oxyhalides:

$$RAsX_4 + 3H_2O \longrightarrow RAsO(OH)_2 + 4HX$$
$$RAsOX_2 + 2H_2O \longrightarrow RAsO(OH)_2 + 2HX.$$

Meyer's reaction has not been found applicable in the synthesis of aromatic arsonic acids, the only exception being benzylarsonic acid.

The unsubstituted arylarsonic acids are well-defined crystalline substances soluble in hot water or alcohol and insoluble in ether. They are very stable, some remaining unaffected even upon boiling with concentrated nitric acid. The degree of firmness with which the arsenic is attached to the nucleus depends upon the nature of the other substituents present, but is practically always quite high. In many cases heating above the melting point causes a loss of one molecule of water with the formation of the corresponding anhydrides, which are reconverted into the acids by warming with water:

$$RAsO(OH)_2 \rightleftarrows RAsO_2 + H_2O.$$

This dehydration occurs much less readily if negative groups are present in the nucleus. Upon fusing with potassium hydroxide the arsono group is replaced by a hydroxyl. Mild reducing agents such as sulfurous acid in the presence of hydriodic acid convert the arsonic acids into the corresponding arsineoxides; stronger reducing agents, e. g., sodium hydrosulfite in alkaline medium at 55-60°, or heating with phosphorous acid in sealed tubes, produce arseno compounds; nascent hydrogen causes a further reduction to the primary arsines, while with hydrogen sulfide arylarsine sulfur compounds result. The acids are not affected by chlorine or bromine, but may be readily nitrated to nitroarylarsonic acids which are reduced to dinitroarsenobenzenes by phosphorous acid and to diaminoarsenobenzenes by warming with sodium hydrosulfite in alkaline solution. Benzylarsonic acid furnishes an exception to the

other members of this group in that it is readily decomposed by mineral acids.

The arylarsonic acids readily form salts: the alkali and alkali earth compounds are generally soluble, crystalline acid salts, while the heavy metal derivatives are insoluble neutral compounds. In practically no case is a precipitate obtained with magnesia mixture in the cold, but upon heating a magnesium salt settles out. The same phenomenon is observed with ammoniacal calcium chloride solution, and constitutes a characteristic distinction from the pentavalent inorganic arsenicals.

Esters may be prepared by two general methods:

1. From sodium alkoxides and arylarsineoxychlorides, e. g.,

$$C_6H_5AsOCl_2 + 2RONa \longrightarrow C_6H_5AsO(OR)_2 + 2NaCl;$$

2. By double decomposition between alkyl iodides and silver arsonates, e. g.,

$$C_6H_5AsO(OAg)_2 + 2RI \longrightarrow C_6H_5AsO(OR)_2 + 2AgI.$$

The last reaction occurs in dry ether medium even at ordinary temperatures but is completed in a reflux apparatus. A calculated amount of the alkyl iodide must be employed since an excess results in the formation of alkyl-arylarsenites and free iodine, e. g.,

$$C_6H_5AsO(OAg)_2 + 4CH_3I \longrightarrow C_6H_5As(OCH_3)_2 + 2AgI + I_2 + (CH_3)_2O.$$

The esters are liquids with disagreeable odors, and are readily hydrolyzed by water into the arsonic acid and the respective alcohol.

Phenylarsonic acid, $C_6H_5AsO(OH)_2$, has been prepared by adding potassium arsenite to an aqueous solution of potassium benzeneisodiazo oxide, stirring and warming until the evolution of nitrogen is complete. After neutralizing the excess of alkali with acid, the liquid is filtered, the filtrate evaporated to dryness and potassium phenylarsonate extracted from the residue by means of alcohol. The salt is then dissolved in water and the free acid isolated by neutralizing with hydrochloric acid.[86] The compound has also been obtained from benzenediazonium chloride and sodium arsenite in the presence of cuprous oxide, without an excess of alkali;[869] from the same diazo compound and an aqueous or dilute alcoholic solution of arsenious acid in a cold or warm acid, neutral or alkaline medium in the presence of two catalysts, one consisting of a copper salt and the other a reducing agent capable of acting in the selected medium;[89] or by Schmidt's modification of Bart's method.[870] The same acid results on diazotizing p-arsanilic acid, introducing into a solution of sodium hypophosphite and hydrochloric acid at a temperature not exceeding 2°, digesting for 18 hours at 2-5° and finally isolating successively through the barium, zinc and

sodium salts.[871] Other methods consist in decomposing phenylarsine-tetrachloride or -oxychloride with water; [446] suspending phenyldichloro-arsine in water and oxidizing with chlorine; [872] or oxidizing phenylarsine with concentrated nitric acid.[873] Finally, it has been obtained in small yields by heating bromobenzene with concentrated aqueous tripotassium arsenite and copper sulfate in a sealed tube at 180-200° for six hours.[874]

Phenylarsonic acid crystallizes in colorless, elongated prisms fairly soluble in cold water, readily in absolute or aqueous alcohol, caustic alkalis or hot water. It softens at 158°, and upon continued heating loses $1H_2O$, yielding the corresponding anhydride. The acid is only slightly soluble in ether, but the latter readily extracts it from aqueous solutions containing an excess of mineral acid. It is a very stable compound, remaining unaffected by hot concentrated nitric or chromic acid. It is reduced to phenylarsine by nascent hydrogen; is decomposed into phenol and potassium arsenite when fused with caustic potash; and yields arsenobenzene upon heating with phosphorous acid in a sealed tube at 180°:

$$2C_6H_5AsO(OH)_2 + 4H_3PO_3 \longrightarrow C_6H_5As = AsC_6H_5 + 4H_3PO_4 + 2H_2O.$$

Salts.—The acid ammonium salt forms crystals which readily effloresce in the air and give off ammonia. The acid potassium salt is a white, amorphous, very hygroscopic substance. The acid barium salt consists of short needles readily soluble in cold water, dilute hydrochloric or nitric acid, less soluble in warm water than in cold. It is prepared by dissolving the acid in baryta water, precipitating the excess barium by means of carbon dioxide and concentrating the filtrate, or by adding first barium chloride and then ammonia to a hot concentrated solution of the arsonic acid. Two calcium salts are known—an acid compound, $(C_6H_5AsO.OH.O)_2Ca$, and a neutral derivative, $C_6H_5AsO_3Ca.2H_2O$. The first, prepared like the corresponding barium salt by employing calcium chloride and ammonia, crystallizes in leaflets with a nacreous luster and a greasy texture; sparingly soluble in either hot or cold water and readily in warm dilute acids. The neutral salt is obtained by cautiously adding ammonia to a cold, dilute aqueous solution containing both phenylarsonic acid and calcium chloride in such a manner that the two liquids do not mix, and allowing to stand for several days. The salt crystallizes out in acicular aggregates with a bright luster and greasy texture.[875] The magnesium salt, $C_6H_5AsO_3Mg$, is prepared by heating a solution of the acid with magnesia mixture.[876] Of the heavy metal derivatives may be mentioned the zinc salt; [877] the copper salt—a blue-green precipitate; the silver salt which separates as a white, microcrystalline powder or platelets with a nacreous luster; and a white, amorphous lead salt, prepared from lead acetate and sodium phenylarsonate. If lead nitrate is employed instead of the acetate, there is obtained a precipitate consisting of lead phenylarsonate and lead

nitrate, from which the latter cannot be removed by washing with hot water.[878] The yohimbine salt melts at 140°.[285] On adding molybdenum trioxide to a hot aqueous solution of sodium phenylarsonate, filtering, concentrating the filtrate and adding guanidinium chloride, there is obtained a mixture of two crystalline compounds which may be separated by hot water.[879] The least soluble compound, consisting of white leaflets, is not affected by boiling with guanidinium carbonate and corresponds to the formula, $(CN_3H_6)H\left[As\begin{matrix} C_6H_5 \\ (MoO_4)_3 \end{matrix}\right].H_2O$. The more soluble derivative, $(CN_3H_6)_5H_5\left[\begin{array}{ccccc} & C_6H_5 & & C_6H_5 & \\ As & & & & As \\ & (MoO_4)_4 & & (MoO_4)_4 & \\ & & MoO_4 & & \end{array}\right].6H_2O$, crystallizes in white needles which, when gently heated with guanidinium carbonate, yield microscopic, hexagonal plates of the formula,

$$(CN_3H_6)_6H_2\left[\begin{array}{ccccc} & C_6H_5 & & C_6H_5 & \\ As & & & & As \\ . & (MoO_4)_3 & & (MoO_4)_3 & . \\ OH & & & & OH \\ & & MoO_4 & & \end{array}\right].4H_2O.$$

Esters.—Methyl phenylarsonate, $C_6H_5AsO(OCH_3)_2$, is a colorless liquid with an unpleasant odor; b. p. 188°/95 mm.; d, 1.3946/23°; readily hydrolyzed by water. The ethyl ester boils at 168-70°/15 mm.; d, 1.318/15°; and is converted by chlorine into phenylarsineoxychloride, chloral and hydrochloric acid.[880]

Phenylarsonic anhydride, $C_6H_5AsO_2$, is a white amorphous powder which on continued heating decomposes without melting. It is readily transformed into the arsonic acid by dissolving in water.[881, 882]

2-Methylphenylarsonic acid, $CH_3.C_6H_4AsO(OH)_2$, is prepared by the action of water on the corresponding arsinetetrachloride or -oxychloride,[883, 884] or from o-toluidine by Bart's reaction.[885] It crystallizes in colorless needles melting at 160°, but when maintained at this temperature for some time, it gradually loses $1H_2O$, yielding the anhydride. Its calcium and barium salts are white crystalline solids; the silver salt is a white, amorphous precipitate slightly soluble in water or dilute alcohol.[886]

3-Methylphenylarsonic acid, from the corresponding arsinetetrachloride and water, crystallizes from hot water in acicular aggregates, m. p. 150°. It is distinguished from its ortho and para isomers in that it melts

in hot water before dissolving, while its isomers do not. At 220-30° it loses one molecule of water, forming the anhydride. Its alkali and alkali earth salts are easily soluble in water; the ammonium salt consists of crystalline crusts; the calcium salt is characterized by its ready solubility in cold but difficult solubility in hot water. A white silver salt, a pale blue copper salt, as well as tin, lead, iron and cobalt compounds have also been prepared. The phenylhydrazine salt,

$$C_7H_7AsO.OH.ONH_3.NHC_6H_5,$$

prepared from the acid and phenylhydrazine in aqueous medium, crystallizes from alcohol in lustrous leaflets.[887]

4-Methylphenylarsonic acid is prepared by treating the corresponding arsinetetrachloride or -oxychloride with water;[883, 888] from p-toluidine by Bart's reaction,[86] or Mouneyrat's modification of the same,[89] or by oxidizing 4-methylphenyldichloroarsine with either chlorine in aqueous medium, hydrogen peroxide in glacial acetic acid solution or with nitric acid.[889] It consists of elongated needles darkening at 300° without melting and losing $1H_2O$ at 105-10° with the formation of the anhydride. Potassium permanganate in alkaline solution oxidizes it to 4-carboxyphenylarsonic acid. Its acid potassium salt is a white deliquescent powder; the acid barium salt forms white needles; the acid calcium salt crystallizes in lustrous leaflets with a greasy texture; the neutral silver salt is a white precipitate which can be obtained crystalline from hot dilute alcohol; the neutral copper salt is blue-green, while the corresponding lead salt is white.[890]

Benzylarsonic acid, $C_6H_5CH_2AsO(OH)_2$, is prepared by Meyer's reaction from benzyl iodide and potassium arsenite,[891] or from benzyl chloride and sodium arsenite.[892] It forms white, lustrous needles, m. p. 167°; sparingly soluble in cold water but readily in alcohol or hot water. It is odorless; has an irritating effect upon the epidermis and mucous membranes, and has a peculiar bitter taste. Unlike the other arsonic acids it is easily decomposed by mineral acids—with concentrated hydrochloric acid benzyl chloride and arsenious acid are formed:

$$2C_6H_5CH_2AsO(OH)_2 + 2HCl \longrightarrow 2C_6H_5CH_2Cl + As_2O_3 + 3H_2O,$$

while with sulfuric acid dibenzyl, benzaldehyde and arsenious acid are obtained:

$$4C_6H_5CH_2AsO(OH)_2 \longrightarrow (C_6H_5CH_2)_2 + 2C_6H_5CHO + 2As_2O_3 + 4H_2O.$$

2,4-Dimethylphenylarsonic acid, $(CH_3)_2C_6H_3AsO(OH)_2$, separates from dilute alcohol as rectangular crystals melting at 210°. The acid ammonium, neutral silver, copper, lead, cobalt and iron salts have been prepared.[575]

2,5-Dimethylphenylarsonic acid crystallizes from hot water in elongated needles, m. p. 223°; readily soluble in hot water or alcohol, sparingly in cold water. Its neutral silver, lead, copper and ferrous salts are insoluble in water.[554]

2,4,5-Trimethylphenylarsonic acid, $(CH_3)_3C_6H_2AsO(OH)_2$, consists of white needles, m. p. 224°; readily soluble in hot water or alcohol. It forms a neutral silver salt.[459]

4-Isopropylphenylarsonic acid, $(CH_3)_2CH.C_6H_4AsO(OH)_2$, exists as lustrous, snow-white needles, m. p. 152°; readily soluble in hot water or alcohol, and yielding 4-carboxyphenylarsonic acid when oxidized with potassium permanganate in alkaline solution.[459]

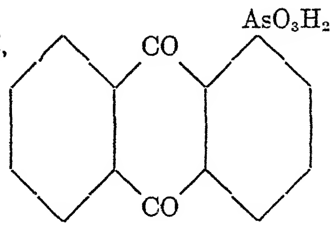
Tertiary-butylphenylarsonic acid, $(CH_3)_3C.C_6H_4AsO(OH)_2$, crystallizes in tufts of needles, m. p. 193°; readily soluble in alcohol, sparingly in hot water. It forms a white, amorphous, neutral silver salt.[460]

4-Phenylphenylarsonic acid, $(C_6H_5)C_6H_4AsO(OH)_2$, is prepared from the corresponding dichloroarsine by oxidation with hydrogen peroxide in glacial acetic acid.[893] It is also formed as a by-product in the preparation of phenylarsonic acid from aniline by Schmidt's modification of Bart's method.[870] The compound separates from water or dilute alcohol as an almost colorless, crystalline powder, m. p. 275° (L.), unmelted up to 300° (S.); readily soluble in alcohol, caustic alkalis or ammonia.

α-Naphthylarsonic acid, $C_{10}H_7AsO(OH)_2$, is obtained either from the arsinetetrachloride in the usual manner[462] or from α-naphthylamine by Bart's reaction.[41] It forms colorless needles melting at 197°, soluble in hot water, acetone, methyl or ethyl alcohol and insoluble in mineral acids, benzene, carbon bisulfide, carbon tetrachloride, chloroform, toluene or xylene. When treated with fuming sulfuric acid (d, 1.9), it yields

?-sulfonaphthylarsonic acid, $C_{10}H_6\begin{cases} AsO_3H_2 \\ SO_3H \end{cases}$, which crystallizes from water in glistening white, slightly hygroscopic plates easily soluble in hot water, alkalis, acetone, methyl or ethyl alcohol, difficultly so in ether and insoluble in mineral acids or the other organic solvents. It neither melts nor decomposes below 250°, and yields upon oxidation a viscous liquid of indefinite composition.[41]

β-Naphthylarsonic acid consists of needles, m. p. 155°; readily soluble in alcohol or hot water.[576]

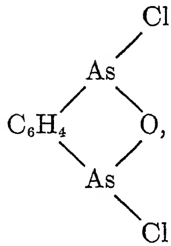
Anthraquinone-α-arsonic acid,  , is derived from α-aminoanthraquinone by Bart's method. It crystallizes from 75 per cent acetic acid in colorless needles difficultly soluble in hot water, almost insoluble in methyl or ethyl alcohol and easily soluble in concentrated sulfuric acid, 2N-sodium carbonate, N-sodium hydroxide or warm 2N-sodium acetate. The acid is reduced to the arseno derivative by warming with sodium hydrosulfite in alkaline solution, but with sodium amalgam the arsenic is split off, yielding anthraquinone. Upon heating on a sand bath the arsonic acid decomposes with the formation of arsenious acid and erythrohydroxyanthraquinone. The sodium, barium, calcium and magnesium salts have been prepared.[894]

The β-*isomer,* similarly prepared, crystallizes in faintly yellow needles which do not melt up to 270°. It is slightly soluble in boiling water, readily in ammonia, concentrated sulfuric acid, 2N-sodium carbonate, N-sodium hydroxide or hot alcohol. Magnesia mixture added to the ammoniacal solution produces an amorphous precipitate in the cold, while calcium chloride yields a crystalline precipitate. Its alkaline solution is colored deep red when treated with sodium hydrosulfite, and unlike the α-isomer yields but a slight amount of anthraquinone with sodium amalgam, thereby indicating that its arsenic is more firmly attached to the nucleus.[895]

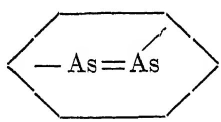
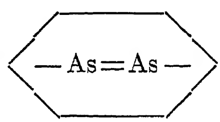
3. *Aryl Diarsonic Acids.—o-Phenylenediarsonic acid,*

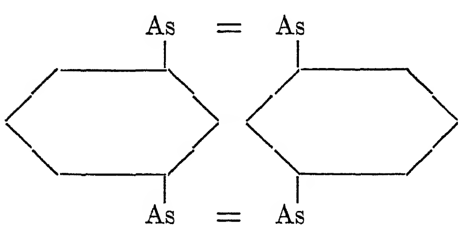
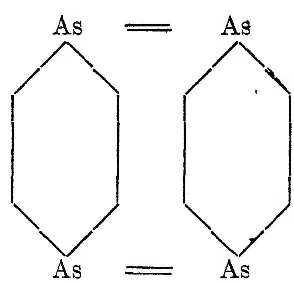
$$C_6H_4(AsO_3H_2)_2,$$

is prepared by treating an alkaline solution of 2-diazophenylarsonic acid with aqueous sodium arsenite in the presence of a little ammoniacal copper sulfate, forming a white, microcrystalline powder containing one molecule of water of crystallization. It is difficultly soluble in water, either very difficultly so or entirely insoluble in the usual organic solvents, does not melt below 360°, and intumesces slightly on strongly heating in the test tube. When warmed with dilute copper sulfate it yields a very bright insoluble copper salt, while boiling bisulfate solution converts it, after temporarily going into solution, into an insoluble arsineoxide.[896] Upon treating a solution of the acid in warm fuming hydrochloric acid with a little aqueous potassium iodide and introducing sulfur dioxide, there are ultimately obtained almost colorless, tetragonal

plates of the *oxychloride,* , which melts at 148°, and is very easily soluble in hot ether, benzene or carbon bisulfide.[897]

m-Phenylenediarsonic acid is derived from m-arsanilic acid by Bart's method, and forms colorless leaflets easily soluble in water or 96 per cent alcohol, difficultly in ethyl acetate and almost insoluble in acetone or ether. It has no melting point, but is decomposed at high temperatures with intumescence. The sodium salt crystallizes with 10 molecules of water.[898] Upon reducing this acid or its p-isomer with phosphorous acid in a sealed tube at 220-35° and 210-20° respectively for several hours, there are produced yellow, amorphous compounds insoluble in the ordinary organic solvents and decomposing at high temperatures. It has not yet been determined whether the formulas of these are

 and , or

 and 

respectively. They are readily oxidized by hydrogen peroxide, more violently by warm dilute or cold concentrated nitric acid, to the corresponding diarsonic acids. On boiling with amyl alcohol they dissolve, separating on cooling as colorless amorphous products.[899]

p-Phenylenediarsonic acid is obtained from atoxyl by Bart's method as above, and crystallizes in colorless, frequently needle-shaped, leaflets quite soluble in water, difficultly so in alcohol and insoluble in ether, acetone or benzene. Its alkali salts are readily soluble in water, but only sparingly in alcohol.[86, 900]

4. *Halogenated Aryl Arsonic Acids.*—Compounds of this group are generally derived:

1. From halogenated arylamines either by Bart's reaction or Mouneyrat's modification of the same.

2. From diazo aminoarylarsonic acids by employing Gattermann's modification of Sandmeyer's reaction.

A very singular method, applicable only to the preparation of mono- and dichloro-2,4-dimethylphenylarsonic acids, consists in treating the corresponding dichloroarsine with chlorine, which causes simultaneous chlorination and oxidation to the arsonic acid.

The halogenated arsonic acids are crystalline solids which, as a rule, are difficultly soluble in cold water, but dissolve more readily in hot water or various organic solvents.

4-Iodophenylarsonic acid serves as the starting material for the preparation of several interesting compounds. Thus, with chlorine it forms an addition product, 4-iodochloride phenylarsonic acid, which is converted into an iodoso compound by the action of caustic soda:

$$H_2O_3AsC_6H_4I + Cl_2 \longrightarrow H_2O_3AsC_6H_4ICl_2$$
$$H_2O_3AsC_6H_4ICl_2 + 2NaOH \longrightarrow H_2O_3AsC_6H_4IO + 2NaCl + H_2O.$$

On treating the iodo or iodoso compound with sodium hypochlorite, oxidation to the iodoxy derivative occurs:

$$H_2O_3AsC_6H_4IO + NaClO \longrightarrow H_2O_3AsC_6H_4IO_2 + NaCl$$
$$H_2O_3AsC_6H_4I + 2NaClO \longrightarrow H_2O_3AsC_6H_4IO_2 + 2NaCl.$$

Both the iodoso and iodoxy compounds are strong oxidizing agents, and decompose violently when heated.

2-Chlorophenylarsonic acid, $ClC_6H_4AsO_3H_2$, is prepared from 2-chloroaniline by Bart's method.[901]

4-Chlorophenylarsonic acid is obtained either by adding copper powder to a hydrochloric acid solution of 4-diazophenylarsonic acid at 0° and subsequently precipitating as the copper salt,[902] or from 4-chloroaniline by Mouneyrat's modification of Bart's method.[89] The compound is characterized by its barium salt, $[ClC_6H_4AsO.OH.O]_2Ba$, which crystallizes in white leaflets upon boiling a suspension of the copper salt with barium hydroxide, removing the excess of barium with carbon dioxide, and concentrating the filtrate.

2-Bromophenylarsonic acid, made from 2-bromoaniline hydrochloride by Bart's process, separates as white leaflets difficultly soluble in water.[903]

4-Bromophenylarsonic acid may be prepared from 4-bromoaniline either by Bart's method,[86] or by Mouneyrat's modification.[89] It crystallizes in the form of white needles sparingly soluble in water, but readily in methyl or ethyl alcohol.

4-Iodophenylarsonic acid is formed, along with some 4-iodophenyldiiodoarsine, as a yellow precipitate on slowly adding to 4-diazophenylarsonic acid a solution of potassium iodide, copper sulfate and sodium thiosulfate in hydrochloric acid. Recrystallized from alcohol, the acid forms fine reddish-white needles soluble in alkali hydroxides or carbonates, hot alcohol, acetone or acetic acid, sparingly in water, alcohol or carbon bisulfide and insoluble in benzene, ether, chloroform, ethyl acetate, petroleum ether or toluene. It is not precipitated from ammoniacal solution by magnesia mixture.[465]

4-Iodochloride phenylarsonic acid, $H_2O_3AsC_6H_4ICl_2$, crystallizes as a yellow powder when a glacial acetic acid solution of 4-iodophenylarsonic acid is saturated with chlorine.[904]

4-Iodosophenylarsonic acid, $H_2O_3AsC_6H_4IO$, results upon dissolving the preceding compound in dilute caustic soda and precipitating with dilute hydrochloric acid. It is a white, microcrystalline substance readily soluble in alkalis or sodium acetate but sparingly so in alcohol, acetic acid or water. It explodes on heating, and is a powerful oxidizing agent, liberating iodine from an acetic acid solution of potassium iodide, decomposing litmus and bleaching indigo.[905]

4-Iodoxyphenylarsonic acid, $H_2O_3AsC_6H_4IO_2$.—When a cold solution of 4-iodophenylarsonic acid in N-sodium hydroxide is saturated with chlorine and then acidified with dilute sulfuric acid, a white granular precipitate is obtained whose oxidizing power surpasses that of the iodoso compound. It explodes sharply when heated and is practically insoluble in the ordinary organic solvents.[905]

4-Chloro-2-methylphenylarsonic acid, $ClC_6H_3(CH_3)AsO(OH)_2$, obtained from the corresponding chlorotoluidine by Bart's method, is precipitated as the magnesium salt, from which the free acid can be isolated by decomposing with hydrochloric acid. The product, m. p. 199°, is readily soluble in hot water but sparingly in cold.[906]

4-Chloro-3-methylphenylarsonic acid is prepared by decomposing the diazo solution of the corresponding amino acid with cuprous chloride. It crystallizes from alcohol in needles melting at 180°.[907]

?-Chloro-2,4-dimethylphenylarsonic acid, $ClC_6H_2(CH_3)_2AsO(OH)_2$, is deposited as needles, m. p. 165°, on passing chlorine into an aqueous suspension of the corresponding dichloroarsine.[908]

2,4-Dichlorophenylarsonic acid, $Cl_2C_6H_3AsO_3H_2$, obtained from 2,4-dichloroaniline by Bart's method, crystallizes from water in fine needles.[909]

3,5-Dichlorophenylarsonic acid.—An intimate mixture of 3,5-dichloro-p-arsanilic acid and potassium pyrosulfite is gradually introduced into ice-cold nitric acid (d, 1.49), and a solution of the diazo compound obtained by the addition of ice. The clear liquid is then warmed with alcohol and a little finely divided copper until the evolution of nitrogen is complete, when, upon cooling, the dichloro acid separates as well-defined, snow-white leaflets soluble in hot water, methyl or ethyl alcohol but sparingly in cold water.[910]

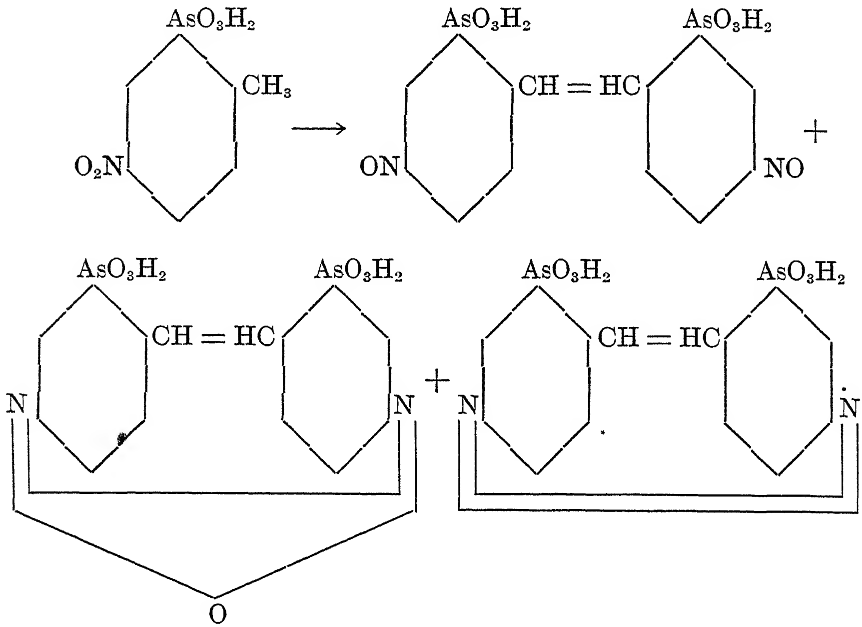
?-Dichloro-2,4-dimethylphenylarsonic acid, $Cl_2C_6H(CH_3)_2AsO(OH)_2$.—Formed on passing chlorine through a solution of the corresponding dichloroarsine in glacial acetic acid. It can be recrystallized from dilute alcohol and melts at 193°.[908]

3,5-Dichloro-4-iodophenylarsonic acid, $(Cl_2)(I)C_6H_2AsO(OH)_2$.—The diazo solution obtained in the preparation of 3,5-dichlorophenylarsonic acid is allowed to crystallize, the resulting crystals redissolved in water, and treated with 10 per cent potassium iodide solution until the evolution of nitrogen ceases, when the desired acid separates out. It crystallizes from 50 per cent acetic acid in white felted needles sparingly soluble in either hot or cold water.[648]

5. *Nitro Aryl Arsonic Acids.*—Nitro groups may be readily introduced into the nuclei of aromatic arsonic acids by the usual methods of nitration. The same products are obtained by treating nitroarylamines either according to Bart's original method, Mouneyrat's modification of this procedure, or H. Schmidt's variation, in which potassium instead of sodium arsenite is employed. The acids are crystalline solids sparingly soluble in cold water, alcohol or acetic acid, but more readily so on heating. With certain reducing agents, such as stannous chloride in hydrochloric acid, the nitro groups alone are reduced, forming amino arsonic acids; reagents like phosphorous acid reduce only the arsonic acid group, yielding the corresponding nitro arseno compound, while with strong reducing agents, such as sodium hydrosulfite in warm alkaline solution, both the nitro and arsonic acid groups are reduced, resulting in the production of aminoarseno derivatives.

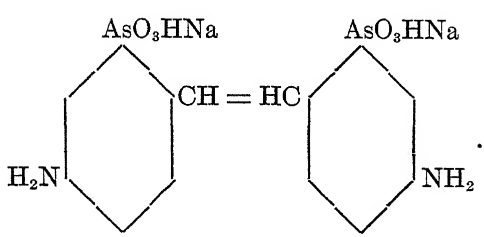
When a nitromethylphenylarsonic acid, in which the nitro group is in para position to the methyl, is warmed with concentrated aqueous sodium hydroxide solution, it yields a mixture of dinitroso-, azoxy-,

and azostilbenediarsonic acids, which are analogous in structure to such commercial dyes as Mikado-Brown, Mikado-Orange and Turmeric:

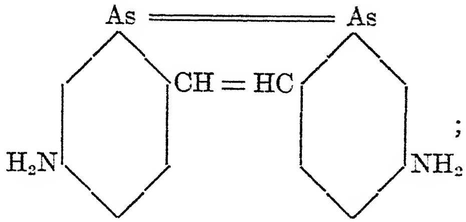


This reduction of the nitro group to nitroso, etc., can be prevented by the addition of an oxidizing agent such as sodium hypochlorite. Thus, 5-nitro-2-methylphenylarsonic acid, when boiled with sodium hydroxide and sodium hypochlorite, yields 5,5′-dinitro-2,2′-stilbenediarsonic acid.

By reducing the mixture of the above stilbene compounds in alkaline solution first with zinc dust and then with sodium hydrosulfite, there is obtained a single product consisting of the disodium salt of diaminostilbenediarsonic acid, whose structure may be represented as follows:



The latter may be further reduced with sodium hydrosulfite to form the corresponding arseno stilbene,



or it may be diazotized and the diazo groups replaced by hydroxyls, producing the corresponding dihydroxystilbenediarsonic acid, which upon reduction is converted into the arseno derivative.

2-Nitrophenylarsonic acid, $O_2N.C_6H_4AsO(OH)_2$, is obtained from o-nitraniline either by Bart's method.[86, 911] or by H. Schmidt's modification of the same.[912] When recrystallized from water, it separates as pale yellow, glistening, hexagonal plates (Jacobs) or almost colorless needles (Bart, Schmidt) containing one molecule of water of crystallization. The anhydrous acid melts with decomposition at 235-40° (J.) or 232° (S.), is soluble in hot alcohol but sparingly in cold alcohol, chloroform or acetone. The acid does not give any precipitate on boiling with magnesia mixture, the magnesium salt separating only on prolonged standing at ordinary temperature. The hydrated acid is readily soluble in hot water, sparingly in cold and slightly in acetic acid, crystallizing from the latter in a practically insoluble, presumably dehydrated modification.

3-Nitrophenylarsonic acid results upon nitrating phenylarsonic acid with either 100 per cent nitric acid or a mixture of concentrated sulfuric and nitric acids.[872] If, however, the latter nitration be conducted in a sealed tube at 155-65° for 3 hours, there is also obtained a small amount of an isomer, which does not dissolve in hot water.[880] A third method consists in treating m-nitraniline according to Schmidt's modification of Bart's method.[913]

The constitution of the above acid has been established by the fact that it is identical with the 3-nitrophenylarsonic acid obtained by the following two methods: (a) 3-nitro-p-arsanilic acid is diazotized, treated with a hydrochloric acid solution of sodium hypophosphite, and the 3-nitrophenylarsonic acid isolated successively through the barium, zinc, and sodium salts.[914] (b) p-Nitranilinearsonic acid is diazotized and the diazo-solution treated with alcohol and copper-bronze. When the evolution of nitrogen has ceased, the filtrate is concentrated and treated with strong caustic soda until faintly acid to congo, the 3-nitro-acid crystallizing out on cooling.[915]

The product consists of leaflets readily soluble in alcohol or hot water, less so in cold water, slightly in benzene or chloroform and

insoluble in ether or ligroin. At 180° it loses water, and carbonizes above 230° without previous melting. If, however, the tube containing the acid is suddenly introduced into sulfuric acid heated to 200°, it melts at once and then quickly resolidifies to the anhydride. Heated with bromine water at 200° it decomposes, yielding 2-nitrobromobenzene, hydrobromic and arsenic acids. With tin and hydrochloric acid an unidentified, dark, amorphous mass is obtained; with stannous chloride and hydrochloric acid Michaelis on one occasion obtained a crystalline double salt of 3-aminophenylarsonic acid and stannous chloride, $(HCl.H_2N)C_6H_4AsO_3H_2.SnCl_2.4H_2O$, while phosphorous acid reduces the nitroarsonic acid to the corresponding nitroarseno derivative.

Salts.—The alkali salts are not crystallizable. Upon concentrating a solution of the diammonium salt, half of the ammonia splits off, leaving the acid salt. The calcium salt, obtained by treating an aqueous solution of the acid with calcium carbonate and boiling the filtrate, crystallizes in fine lustrous leaflets which do not lose their water of crystallization even at 110°, probably due to their constitution which may be represented by the following formula, $O_2N.C_6H_4As\begin{cases} =O \\ -OH \\ -O.Ca(OH) \end{cases}$. The barium salt, $[O_2N.C_6H_4AsO.OH.O]_2Ba$, crystallizes in crusts; the cupric salt is a blue crystalline substance whose water of crystallization cannot be removed by heating; the silver salt is a white amorphous deposit easily soluble in ammonia or nitric acid; the magnesium salt may be obtained by boiling the acid with magnesia mixture.[916]

4-Nitrophenylarsonic acid, from p-nitraniline by Bart's method,[86] crystallizes from water in pale yellow aggregates of minute leaflets which do not melt below 275°, are sparingly soluble in hot methyl alcohol or acetic acid, cold water or ethyl alcohol, but dissolve readily in the latter on heating.[917]

4-Nitro-2 or 6-methylphenylarsonic acid, $O_2N.C_6H_3(CH_3)AsO(OH)_2$, is prepared from 5-nitro-o-toluidine by Bart's reaction, forming almost colorless needles melting with decomposition at 235-40°. It is readily soluble in hot water, alcohol or acetic acid and practically insoluble in acetone or chloroform.[918]

5-Nitro-2-methylphenylarsonic acid may be obtained by nitrating the corresponding arsonic acid with nitric-sulfuric acid at 20-35°,[919] or from 4-nitro-o-toluidine by Bart's reaction.[920] It forms white felted needles darkening at 230° and melting at 261° (Karrer), or pale yellow, glistening plates melting at 225° with the evolution of a gas, then resolidifying

and finally melting with decomposition at 261-3° (Jacobs). It is very sparingly soluble in cold water, alcohol or acetic acid, though readily on heating; is soluble in methyl alcohol but practically insoluble in acetone or chloroform. When heated with aqueous alkalis at 90° for 15 minutes, it undergoes a complicated series of reactions, yielding a mixture of dinitroso-, azoxy- and azostilbenediarsonic acids, which is soluble in alkalis but not in the usual solvents.[921]

5,5'-Dinitro-2,2'-stilbenediarsonic acid,

$$(H_2O_3As)(O_2N)C_6H_3.CH = HC.C_6H_3(NO_2)(AsO_3H_2),$$

results upon warming the preceding arsonic acid with aqueous sodium hydroxide and hypochlorite for five minutes at 90° and then acidifying with concentrated hydrochloric acid. It separates as a white crystalline precipitate sparingly soluble in water or alcohol. Warming its alkaline solution with a little acetone produces a reddish-brown condensation product, but with phenylhydrazine—merely a red coloration.[919]

6-Nitro-2-methylphenylarsonic acid is prepared from 3-nitro-o-toluidine by Bart's method, and, when recrystallized from hot water, separates as star-shaped aggregates of pale yellow, delicate needles decomposing at 228-30°. It is practically insoluble in cold water, sparingly in hot, more soluble in hot alcohol or glacial acetic acid and readily in methyl alcohol.[922]

2 or 6-Nitro-4-methylphenylarsonic acid, which results on treating 3-nitro-p-toluidine according to Bart's method, forms faintly yellow, minute rods, m. p. 255-60° with decomposition; very sparingly soluble in cold water, alcohol or acetic acid but more soluble on boiling.[922]

3 or 5-Nitro-4-methylphenylarsonic acid may be obtained either from 2-nitro-p-toluidine by Bart's reaction,[923] or by slowly nitrating 4-methylphenylarsonic acid with a mixture of concentrated sulfuric and fuming nitric acids at low temperature.[924] It crystallizes from hot water in lustrous needles which do not melt below 300° and intumesce at higher temperatures. The acid is readily soluble in hot water, acetic acid, methyl or ethyl alcohol, less so in benzene or chloroform, difficultly in cold water, acetic acid or acetone and insoluble in ligroin or ether. When heated it loses water, but decomposition begins before one molecule is split off.

Salts.—The alkali salts are not crystallizable; the silver salt is a white amorphous powder; the barium salt consists of small white needles, while the calcium and cobalt salts form small lustrous leaflets and violet crystals respectively. The latter two, together with the cupric salt, have the same general composition, $O_2N.C_6H_3(CH_3)AsO_3R.H_2O$,

the molecule of water being so firmly held that it cannot be removed without partial decomposition of the salts.[925]

?-*Nitro-2,4-dimethylphenylarsonic acid,* $O_2N.C_6H_2(CH_3)_2AsO(OH)_2$, prepared by nitrating the corresponding arsonic acid with fuming nitric acid at low temperature, crystallizes in short, white needles melting at 207°, decomposing with intumescence above 306° and readily soluble in water, though less so in alcohol or ether. Its silver salt has been prepared.[575]

?-*Nitro-2,5-dimethylphenylarsonic acid,* similarly produced, crystallizes from alcohol in white needles, m. p. 205°; difficultly soluble in water but much more easily in alcohol. On heating with phosphorous acid in a sealed tube, the corresponding arseno-compound is obtained.[554]

4-Nitro-2,5-dimethylphenylarsonic acid is obtained from 2,5-dimethyl-p-nitraniline by Bart's reaction. It crystallizes from 50 per cent acetic acid in pale yellow, spindle-shaped prisms, wedge-shaped platelets, or long, flat plates melting with decomposition at 290°, sparingly soluble in boiling water but readily so in hot alcohol or acetic acid. It is not identical with the preceding isomer.[926]

4-Nitro-α-naphthylarsonic acid, $O_2N.C_{10}H_6AsO(OH)_2$, from α-napthylarsonic acid and warm nitric acid (d, 1.4), separates from alcohol in small, pale yellow needles soluble in methyl, less so in ethyl alcohol, difficultly in hot water and practically insoluble in cold. Mineral acids produce a precipitate which redissolves in an excess of the reagent. The arsenic is completely removed either by heating with concentrated hydrochloric acid at 120° for 3-4 hours; by fusion with solid potassium hydroxide; or by treatment with phosphorus pentachloride, but only to a slight extent by bromine and not at all by iodine.[590]

4-Chloro-3-nitrophenylarsonic acid, $(O_2N)(Cl)C_6H_3AsO(OH)_2$, is prepared from 4-chloro-m-nitraniline by Mouneyrat's modification of Bart's method,[89] or by nitrating 4-chlorophenylarsonic acid,[907] and crystallizes from dilute alcohol in the form of white leaflets which on heating decompose with intumescence. On boiling with aqueous caustic potash, the chlorine is replaced by a hydroxyl.

6-Chloro-3-nitrophenylarsonic acid, made by nitrating 2-chlorophenylarsonic acid, consists of white needles difficultly soluble in water, easily in hot alcohol and intumescing on heating.[901]

4-Bromo-3-nitrophenylarsonic acid may be prepared from 4-bromoaniline by Mouneyrat's modification of Bart's method.[89]

4-Chloro-5-nitro-2-methylphenylarsonic acid,

$$(Cl)(O_2N)C_6H_2(CH_3)AsO(OH)_2,$$

separates in white, lustrous leaflets on nitrating the corresponding arsonic acid with nitric-sulfuric acid at 30-40°, but when recrystallized from water, it forms beautiful scales melting at 215°. On warming with aqueous caustic soda for 15 minutes, diluting and then acidifying, a flocculent, brown stilbene-dye results.[906]

4,4′-Dichloro-5,5′-dinitro-2,2′-stilbenediarsonic acid,

$$(H_2O_3As)(O_2N)(Cl)C_6H_2.CH=HC.C_6H_2(Cl)(NO_2)(AsO_3H_2),$$

a white crystalline powder sparingly soluble in hot water, is obtained upon warming the preceding arsonic acid with sodium hydroxide and hypochlorite at 90° for five minutes and acidifying with hydrochloric acid.[730]

4-Chloro-5-nitro-3-methylphenylarsonic acid is derived from the corresponding arsonic acid by nitration with nitric-sulfuric acid, and crystallizes from alcohol in yellowish needles, m. p. 310°; soluble in dilute aqueous caustic soda.[907]

2,4-Dichloro-5-nitrophenylarsonic acid, $O_2N.Cl_2C_6H_2AsO(OH)_2$, is obtained by nitrating the corresponding dichloro arsonic acid.[909]

2,4-Dinitrophenylarsonic acid, $(O_2N)_2C_6H_3AsO(OH)_2$.—The introduction of arsonic acid groups into aromatic nuclei by Bart's diazo-reaction is usually carried out in alkaline or neutral solution. With diazotized 2,4-dinitroaniline, however, this synthesis does not take place under such conditions, and can only be carried out in the presence of an excess of acid.

2,4-Dinitroaniline is added to a cold mixture of concentrated sulfuric acid and sulfuric acid containing 59% of nitrosylsulfate, the resulting solution poured upon ice, treated with aqueous sodium arsenite, and the evolution of nitrogen completed by heating with steam. After clarifying with animal charcoal, the acid crystallizes in felted needles, m. p. 199-200°; moderately soluble in cold water and readily in aqueous alkalis, sodium acetate, glacial acetic acid, methyl or ethyl alcohol. The aqueous solution turns congo paper violet.[927]

4-Chloro-3,5-dinitrophenylarsonic acid, $(O_2N)_2ClC_6H_2AsO(OH)_2$, is obtained when 4-chloro-3-nitrophenylarsonic acid is energetically nitrated with nitric-sulfuric acid. It consists of white crystals soluble in alcohol, hot water or strong hydrochloric acid.[928]

3-Nitro-?-(m-nitrophenyl)phenylarsonic acid,

$$(O_2N.C_6H_4)C_6H_3(NO_2)AsO(OH)_2.$$

Formed as a by-product in the preparation of 3-nitrophenylarsonic acid from 3-nitraniline. It is a light brown powder soluble in alkali or ammonia and darkening but not melting below 260°. In concentrated solution a precipitate with magnesia mixture results even in the cold, but in dilute solution—only on boiling.[929]

4-Nitrosophenylarsonic acid, $C_6H_4\begin{cases}AsO_3H_2\\NO\end{cases}$.—Atoxyl is gradually introduced into an ice-cold solution of neutral monopersulfuric acid, H_2SO_5 (200 c.c. = 1.67 g. O), the whole rendered slightly alkaline with sodium carbonate, and allowed to stand for 30 minutes. Upon acidifying the filtrate, the nitroso compound separates in yellow crystals readily soluble in alkali hydroxides or carbonates, acetic acid or hot water, sparingly in cold water, methyl or ethyl alcohol, ether, chloroform, pyridine, etc. At 180° it decomposes, and intumesces at higher temperatures. Sulfurous acid reduces it to 4-aminophenylarsineoxide while with sodium hydrosulfite the corresponding diamino arseno compound results. It reacts quantitatively with phenylhydrazine (2 moles), the nitrogen of the latter being completely evolved. The above arsonic acid behaves like a typical nitroso compound: it liberates iodine from acidulated potassium iodide, or sulfur from hydrogen sulfide water; condenses to an intense reddish-brown azo compound when warmed with aniline and acetic acid; yields a brown coloration with ferrous sulfate and concentrated sulfuric acid, and a blue color with diphenylamine sulfuric acid; exhibits the Liebermann reaction with phenol and concentrated sulfuric acid; and with β-naphthol and hydroxylamine yields first a brown and then a red coloration due to the formation of an azo dye.[930] It condenses with p-phenylenediamine or 2,5-diaminophenylarsonic acid in glacial acetic acid medium to form diazo dyes containing arsenic.[931, 932]

3,4-Dinitrosophenylarsonic acid, $(ON)_2C_6H_3AsO_3H_2$, prepared by heating 3-nitro-4-triazophenylarsonic acid up to 73-5°, decomposes at 230°, is soluble in aqueous alkalis, alcohol or glacial acetic acid, but very difficultly so in cold water.[536]

Azoxybenzene-4,4′-diarsonic acid, $H_2O_3AsC_6H_4N\underset{O}{\overset{}{-\!-}}NC_6H_4AsO_3H_2$.—An aqueous solution of atoxyl is oxidized with potassium ferricyanide in alkaline solution, and the azoxy compound isolated as the barium salt. The corresponding disodium salt is a brownish powder.[933]

Hydrazobenzene-2,2'-diarsonic acid,

$$H_2O_3AsC_6H_4NH.NHC_6H_4AsO_3H_2,$$

is produced together with a small amount of 2-aminophenylarsonic acid by the electrolytic reduction of 2-nitrophenylarsonic acid in sodium acetate solution. It is a light brown powder soluble in ammonia or concentrated acids; forms a silver mirror with ammoniacal silver nitrate solution; and oxidizes to the corresponding azo derivative upon exposure to the air.[934]

6. *Amino Aryl Arsonic Acids.*—The compounds resulting from the introduction of an amino radical into primary arsonic acids constitute one of the most important groups of aromatic arsenicals, for their great reactivity renders them invaluable as the parent substances in the synthesis of many other arsenic derivatives. They may be prepared directly from primary amines by condensing with arsenic acid at high temperatures:

$$C_xH_yNH_2 + H_3AsO_4 \longrightarrow C_xH_yNH_2.H_3AsO_4 \longrightarrow$$

$$\begin{matrix} H_2O_3As \\ H_2N \end{matrix} > C_xH_{y-1} + H_2O.$$

In this procedure known as the Béchamp reaction, the arsenic enters the ring in the position para to the amino group. However, if this position is already occupied, it either enters the ortho position or no arsenation occurs. The amino acids may also be obtained:

1. By the reduction of the corresponding nitro acids with various reagents, such as ferrous sulfate or chloride and caustic soda, sodium amalgam in methyl alcoholic medium, sodium hydrosulfite at low temperature, or hydrogen under pressure in the presence of palladous hydroxide.
2. By applying Bart's reaction to aromatic diamines.
3. From diaminoarsonic acids by diazotizing with 1 mole of sodium nitrite, and replacing the diazo group with a hydrogen atom by means of copper powder in the presence of alcohol.
4. By hydrolyzing N-acylated aminoarylarsonic acids.

The compounds are colorless, crystalline substances soluble in dilute mineral acids, alkalis, hot water, methyl or ethyl alcohol, sparingly in the latter three solvents at ordinary temperature or glacial acetic acid and generally insoluble in the other organic solvents. With potassium iodide and dilute sulfuric acid they usually yield 4-iodoarylamines. The amino arsonic acids can be readily diazotized and the diazo group replaced by a hydrogen, halogen, hydroxyl or a second arsonic acid radical

The diazo derivatives may be coupled with various amino compounds or azo components, yielding diazo-amino derivatives and azo dyes respectively.

The aminoarylarsonic acids can be readily acylated:

1. By treating anhydrous sodium arsonates with anhydrous acids.
2. By the action of acid anhydrides upon the above salts either in the dry form or in aqueous solution.
3. By allowing arsonic acids to react with acid anhydrides in the presence of either an anhydrous salt of the acid corresponding to the same anhydride or a little concentrated sulfuric acid.
4. As a result of the interaction of acid chlorides and arsonic acids either directly or in the presence of a reagent which combines with the generated hydrochloric acid, such as pyridine or caustic soda.
5. By heating arsonic acids with various esters.

These products are generally well-defined crystalline solids soluble in alkalis, and considerably less basic than the amino acids. Thus, they dissolve in concentrated mineral acids, but are reprecipitated upon dilution with water. They do not exhibit the characteristic reactions of a primary amine, e. g., they cannot be diazotized or condensed with aldehydes or sodium β-naphthoquinonesulfonate. When boiled with concentrated alkalis or mineral acids the acyl radicals are split off.

The amino acids may be alkylated directly by the usual methods, yielding well-defined crystalline products readily soluble in dilute acids or alkalis. The same products are more readily obtained by oxidizing the corresponding arsineoxides with red mercuric oxide in aqueous medium or, even better, with hydrogen peroxide in alkaline solution.

2-Aminophenylarsonic acid (*o-Arsanilic acid*), $H_2N.C_6H_4AsO(OH)_2$, is obtained by hydrolyzing its oxanilide with 2N-sulfuric acid and isolating through the barium salt,[935] or by reducing 2-nitrophenylarsonic acid with either ferrous sulfate[936] or ferrous chloride[151] in alkaline solution. It forms needles, m. p. 153°; readily soluble in water, glacial acetic acid, alkalis, mineral acids, methyl or ethyl alcohol but sparingly in ether. When heated with potassium iodide and dilute sulfuric acid at 80-5° it is converted into 2-iodoaniline. On diazotizing and coupling with R-salt, a reddish-orange dye is obtained, whose color is less intense than those of the dyes derived from the m- and p-isomers. The magnesium salt is obtained only upon boiling the free acid with magnesia mixture, while the silver salt, resulting upon the addition of silver nitrate to the sodium salt, separates at first as a curdy white precipitate which spontaneously changes into well-defined lustrous needles.

The acid is more soluble in water; has a lower melting point; is more toxic and less stable than the p-isomeride. In addition, its arsonic acid group can be replaced by iodine at a lower temperature. When

warmed with benzaldehyde in alcoholic solution, the arsonic acid forms a condensation product, benzylidene-o-arsanilic acid,

$$H_2O_3AsC_6H_4.N = HC.C_6H_5,$$

m. p. 228-30°.[151]

3-Aminophenylarsonic acid (*m-Arsanilic acid*).—Upon reducing 3-nitrophenylarsonic acid with ammonium sulfide, Michaelis had found that both the nitro and arsonic groups were affected, resulting in the formation of 3-aminophenylarsinesulfide.[557] Later Bertheim succeeded in obtaining m-arsanilic acid by treating the above sulfide with copper sulfate in an alkaline medium, and isolating successively through the zinc and sodium salts.[558] The acid may also be prepared by reducing 3-nitrophenylarsonic acid in methyl alcohol with sodium amalgam, distilling off the solvent and isolating the compound either through the zinc salt,[937] or by acidifying with hydrochloric acid, removing the sodium chloride and subsequently neutralizing with sodium acetate.[938] The reduction of the 3-nitro acid may also be effected by means of ferrous hydroxide,[936] or hydrogen in the presence of palladous hydroxide.[901]

Finally, it may be made by diazotizing 2,5-diaminophenylarsonic acid with one mole of sodium nitrite, and replacing the diazo group with hydrogen by means of alcohol and copper powder, the acid remaining in solution. From this it is isolated in pure form by again diazotizing, coupling with β-naphthol in alkaline solution, and treating the resulting dyestuff with sodium hydrosulfite at 25-37°.[939] Recrystallized from water, it forms colorless prisms melting at 214°; less soluble in water than the p-isomer, very sparingly soluble in organic solvents, but readily in mineral acids, alkali hydroxides, carbonates or bicarbonates. Only two salts have been mentioned, a white silver salt and a magnesium salt, the latter being prepared by boiling an ammoniacal solution of the acid with magnesia mixture. It does not couple with diazobenzene or diazosulfanilic acid, but with 4-nitrodiazobenzene it yields a yellow dye soluble in alkali with a red color. The diazotized m-arsanilic acid couples with the usual azo-components, forming azo-dyes readily soluble in soda solution. By warming the acid with acidified potassium iodide no arsenic is split off, while with bromine water it does not yield tribromoaniline, but a bromoaminophenylarsonic acid (distinctions from the para-isomer).

4-Amino-2 or 6-methylphenylarsonic acid,

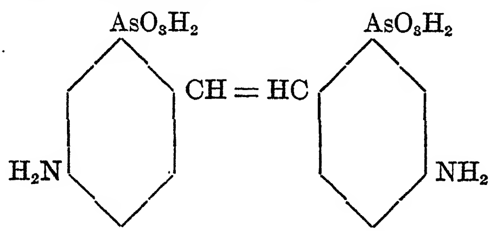
$$H_2N.C_6H_3(CH_3)AsO(OH)_2,$$

is prepared from m-toluidine and arsenic acid by the Béchamp reaction;[940] or by reducing 4-nitro-2 or 6-methylphenylarsonic acid with ferrous sulfate[918] or ferrous chloride[151] and sodium hydroxide. It crystallizes from water in microscopic needles and prisms, m. p. 180°

(Benda) darkening and decomposing at 222-24° (Jacobs). Upon diazotizing and coupling with R-salt it yields an orange-red solution. The acid condenses with benzaldehyde and pyruvic acid forming 1-(4-arsono-3′-methylphenyl)-2-phenyl-4,5-diketopyrrolidine.[151]

5-Amino-2-methylphenylarsonic acid, resulting upon treatment of the corresponding nitro acid with ferrous sulfate and alkali, consists of cream-colored prisms decomposing at 235-45°, sparingly soluble in hot water, acetic acid, methyl or ethyl alcohol. It yields a cherry-red coloration on coupling its diazo solution with R-salt.[918]

5,5′-Diamino-2,2′-stilbenediarsonic acid,



The mixture of dinitroso-, azoxy- and azostilbenediarsonic acids, obtained by warming 5-nitro-2-methylphenylarsonic acid with concentrated aqueous caustic soda, is dissolved in dilute sodium hydroxide and refluxed for 12 hours, during which time zinc dust is gradually introduced. The liquid is then treated with sodium hydrosulfite and filtered into an excess of dilute hydrochloric acid, when the crude product is obtained as a brown amorphous precipitate. This is purified by dissolving in hot aqueous sodium carbonate, decolorizing with sodium hydrosulfite, and transposing the resulting disodium salt with mineral acid. The compound consists of yellow flakes readily soluble in alkalis or excess of mineral acids, and forming a red Schiff base with dimethylaminobenzaldehyde in hydrochloric acid solution. Its disodium salt crystallizes with four molecules of water as bright, iridescent, yellowish-brown leaflets which are very hygroscopic, and dissolve readily in hot but only sparingly in cold water.[941]

6-Amino-2-methylphenylarsonic acid is prepared like its preceding isomer, and crystallizes from hot water in rosets or plates decomposing at 175-80°, soluble in glacial acetic acid, methyl or ethyl alcohol, but less so in acetone or water at ordinary temperature. Its diazo solution does not give a strong color with R-salt.[923, 151]

4-Amino-3-methylphenylarsonic acid may be obtained by condensing o-toluidine with arsenic acid according to the Béchamp reaction. It forms tabular crystals melting at 195° (Benda), 198-200° with decomposition (Wellcome); is sparingly soluble in cold water, or alcohol,

more so on warming, insoluble in ether or benzene and readily soluble in dilute mineral acids, alkali hydroxides or carbonates. It may be diazotized and coupled with phenols. Heating with potassium iodide and dilute sulfuric acid converts the amino arsonic acid into the corresponding iodotoluidine.[942, 940, 943]

The acid forms a cream-colored condensation product with benzaldehyde (*Benzylidene-4-amino-3-methylphenylarsonic acid*),

$$H_2O_3AsC_6H_3\begin{array}{l} \diagup CH_3 \\ \\ \diagdown N = HC.C_6H_5 \end{array},$$

m. p. 202-5° with decomposition, while with 4-chlorobenzaldehyde there is obtained *4′-chlorobenzylidene-4-amino-3-methylphenylarsonic acid*, a pale yellow powder melting at 255-60° with decomposition.[151] The amino acid can be readily converted into the acetylamino derivative by treatment with acetic anhydride.

The sodium salt (*"Kharsin"*), $H_2N.C_6H_3(CH_3)AsO.OH.ONa$, which crystallizes from alcohol with $3\frac{1}{2}H_2O$ and from water with $5H_2O$, is readily soluble in water, sparingly in alcohol and insoluble in ether or benzene.[944]

6-Amino-3-methylphenylarsonic acid, from p-toluidine by direct arsenation at 195-200°, consists of felted needles, m. p. 176°; readily soluble in hot water, methyl or ethyl alcohol, sparingly in cold water, very sparingly in ether and insoluble in benzene.[945]

2 or 6-Amino-4-methylphenylarsonic acid may be obtained by reducing the corresponding nitro compound with ferrous sulfate and sodium hydroxide. It forms colorless needles melting at 180°, readily soluble in water, glacial acetic acid, methyl or ethyl alcohol but sparingly in acetone or ether. When diazotized and coupled with R-salt, it forms a weak orange-red dye.[922]

3-Amino-4-methylphenylarsonic acid, prepared like the previous compound, exists as microscopic needles melting at 172-5°, sparingly soluble in water, acetic acid, methyl or ethyl alcohol at ordinary temperatures, but readily on warming. Its diazo solution gives a cherry-red coloration with R-salt.[923]

4-Amino-2,5-dimethylphenylarsonic acid,

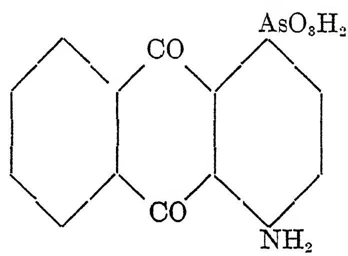
$$H_2N.C_6H_2(CH_3)_2AsO(OH)_2,$$

produced by arsenating p-xylidene,[946] or by reducing the corresponding nitro compound with alkaline ferrous sulfate,[947] crystallizes from water

in practically colorless platelets containing $1H_2O$. The anhydrous substance melts at 215°.

2-Amino-3,5-dimethylphenylarsonic acid, obtained by arsenating m-xylidene, is a microcrystalline powder melting at 199-200°, readily soluble in hot water, methyl or ethyl alcohol, sparingly in cold water and practically insoluble in ether or benzene. When warmed with potassium iodide and dilute sulfuric acid, it is converted into 1-iodo-2-amino-3,5-dimethylbenzene.[948]

4-Amino-α-naphthylarsonic acid, $H_2N.C_{10}H_6AsO(OH)_2$, is derived from dry α-naphthylamine by the Béchamp reaction, and crystallizes in prisms melting at 175°, readily soluble in hot water or alcohol, sparingly in ether and insoluble in chloroform or petroleum. It may be diazotized and coupled with various azo-dye components. The alkali salts are very soluble in water, from which they are precipitated by alcohol.[946, 949, 590]

4-Aminoanthraquinonearsonic acid, ,

is prepared from 1,4-diaminoanthraquinone by Bart's method, and isolated through the sodium salt. It is a vermilion-colored crystalline powder decomposing at 278° without melting, almost insoluble in boiling water, completely so in methyl or ethyl alcohol, and soluble in concentrated ammonia, N-caustic soda, 2N-sodium carbonate or hot sodium acetate, concentrated sulfuric acid or hot 5N-hydrochloric acid, the hydrochloride separating from the latter in reddish-gray crystals. Its diazo compound, best prepared with "Nitrose" * in concentrated sulfuric acid, couples red with R-salt and yellow-orange with resorcin. With magnesia mixture the ammoniacal solution of the arsonic acid gives a red precipitate even in the cold, while barium hydroxide produces a fiery-red precipitate. The sodium salt crystallizes in brick red needles containing water of crystallization and is soluble in hot water.[950]

7. *Derivatives of Amino Aryl Arsonic Acids.—2-diazophenylarsonic acid,* $H_2O_3AsC_6H_4.N=N.OH$, is obtained as a stable, pale yellow liquid by diazotizing a fuming hydrochloric acid solution of o-arsanilic acid with sodium nitrite at —8°.[951]

* A solution of nitrosylsulfuric acid in sulfuric acid, formed in the lead-chamber process.

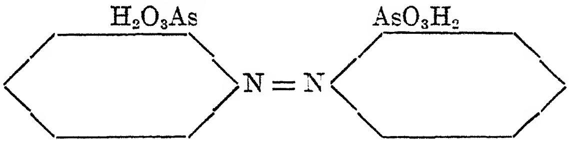
Diazo-2-methylphenyl-(4-arsonic acid)-p-aminophenoxyacetic methyl ester is obtained as a sodium salt by diazotizing 2-methyl-4-aminophenylarsonic acid, adding a large excess of saturated sodium acetate solution and coupling with the hydrochloride of 4-aminophenoxyacetic methyl ester. It crystallizes in spherules of drab, microscopic needles. The *free ester acid* forms flat needles decomposing at 130-2°.

The *free p-aminophenoxyacetic acid derivative* has not been obtained crystalline. Its disodium salt separates from water-alcohol as minute brownish leaflets.[952]

Diazo-2-bromophenyl-(4-arsonic acid)-p-aminophenoxyacetic methyl ester, prepared in a similar manner from diazotized 3-bromo-4-aminophenylarsonic acid and the above amino ester hydrochloride, forms spherules of brownish needles intumescing at 123-5°. The sodium salt crystallizes in pinkish, hair-like, microscopic needles.

The *free p-aminophenoxyacetic acid derivative* is obtained as drab-colored microscopic crystals intumescing at 130°. Its disodium salt consists of spherules of minute crystals.[952]

o-Azobenzenediarsonic acid,



is obtained either by reducing 2-nitrophenylarsonic acid with zinc dust and ammonia in the presence of ammonium chloride, or as a by-product in the preparation of diphenylarsinic acid-o-arsonic acid or o-phenylenediarsonic acid. It crystallizes in yellow to orange-yellow needles, m. p. 272°; soluble in caustic alkali and practically insoluble in water or organic solvents.[953]

m-Azobenzenediarsonic acid.—m-Arsanilic acid is diazotized, treated with sodium arsenite at 0°, slowly warmed up to 40-50°, and finally acidified with hydrochloric acid. On concentrating the filtrate the crude product separates as a reddish-brown powder, which may be purified through the sodium salt. The free acid crystallizes in long, orange-yellow needles very easily soluble in water and not melting below 240°. Its sodium salt consists of orange-yellow needles containing 11 molecules of water of crystallization.[954]

2-Hydroxynaphthaleneazobenzene-3′-arsonic acid,

$$HO.C_{10}H_6.N = N.C_6H_4AsO_3H_2,$$

may be prepared from m-arsanilic acid by diazotizing and coupling with β-naphthol, or indirectly from 2,5-diaminophenylarsonic acid by

diazotizing with one molecular proportion of sodium nitrite, treating with alcohol and copper bronze, diazotizing with another mole of sodium nitrite, and finally coupling with alkaline β-naphthol. The product is a red powder soluble in hot water or dilute aqueous soda. When reduced with alkaline hydrosulfite, it yields m-arsanilic acid.[955]

2-Amino-3,6-disulfonaphthalene-1-azobenzene-3′-arsonic acid,

$$(H_2N)(SO_3H)_2C_{10}H_4.N=N.C_6H_4AsO_3H_2,$$

is formed upon diazotizing m-arsanilic acid and coupling with β-naphthylamine-3,6-disulfonic acid.[581]

4-Dimethylaminobenzene-2′-azotoluene-5′-arsonic acid,

$$(CH_3)_2N.C_6H_4.N=N.C_6H_3(CH_3)AsO_3H_2,$$

results upon diazotizing 4-amino-3-methylphenylarsonic acid (2-aminotolyl-5-arsonic acid), and coupling with dimethylaniline in acid solution. It is a red crystalline powder forming salts with both acids and bases. Its monosodium salt, containing $5H_2O$, is a red crystalline powder moderately soluble in hot water, while the disodium salt is a red powder soluble in cold water, and contains $4H_2O$.[956]

4-Hydroxybenzene-2′-azotoluene-5′-arsonic acid,

$$HO.C_6H_4.N=N.C_6H_3(CH_3)AsO_3H_2,$$

is prepared like the preceding compound by coupling with an alkaline solution of phenol. The product is a light red, crystalline powder practically insoluble in boiling water or the usual organic solvents but readily soluble in alkalis. Its monosodium salt, which crystallizes from water in red leaflets containing $2\frac{1}{2}H_2O$, is sparingly soluble in cold and moderately soluble in hot water. The disodium salt is a water-soluble red powder containing $4\frac{1}{2}H_2O$.[957]

2-Aminoazonaphthalene-4′-arsonic acid,

$$H_2NC_{10}H_6N=NC_{10}H_6AsO_3H_2,$$

obtained as a hydrochloride by diazotizing 4-aminonaphthylarsonic acid and coupling with β-naphthylamine hydrochloride, is a dark red precipitate soluble in excess of aqueous alkali.[590]

4-Sulfoazobenzene-5′-amino-2′-arsonic acid is a light brown powder resulting upon diazotizing sulfanilic acid and coupling with p-arsanilic acid in alkaline solution. The product yields a lustrous, brownish-black powder when diazotized and coupled with an alkaline solution of H acid.[582]

2-Hydroxynaphthaleneazobenzene-2′-hydroxy-4′-arsonic acid,

$$(HO)C_{10}H_6N = NC_6H_3(OH)AsO_3H_2.$$

3-Nitro-4-aminophenylarsonic acid is diazotized, treated with sodium acetate to replace the nitro group by a hydroxyl, and the resulting product coupled with alkaline β-naphthol. The dye acid consists of lustrous red crystals which may be reduced to 4-amino-3-hydroxyphenylarsonic acid either by sodium hydrosulfite at 25-40° or aluminium powder at 40-60°. At 65-70° hydrosulfite reduces the above dye to 4,4′-diamino-3,3′-dihydroxyarsenobenzene.[958]

2,4,6-Trihydroxyazobenzene-6′-hydroxy-3′-arsonic acid,

$$(HO)_3C_6H_2N = NC_6H_3(OH)AsO_3H_2,$$

is prepared by coupling diazotized 3-amino-4-hydroxyphenylarsonic acid with phloroglucinol.[581]

2-Hydroxynaphthaleneazobenzene-6′-hydroxy-3′-arsonic acid is a bright red, alkali-soluble precipitate obtained by diazotizing 3-amino-4-hydroxyphenylarsonic acid and coupling with alkaline β-naphthol.[582]

2-Amino-6-sulfo-8-hydroxynaphthaleneazobenzene-6′-hydroxy-3′-arsonic acid, obtained like the preceding compound by coupling with 2-amino-6-sulfo-8-hydroxynaphthalene (Gamma Acid), is a lustrous, purplish-black powder.[582]

1-Amino-8-hydroxy-3′,6-disulfonaphthaleneazobenzene-6′-hydroxy-3′-arsonic acid.—A lustrous, purplish-black product obtained by treating 4-hydroxy-3-diazophenylarsonic acid with an alkaline solution of H acid.[582]

8. *N-Substituted Derivatives of Amino Aryl Arsonic Acids.—4-Acetylamino-2-methylphenylarsonic acid,* $H_2O_3AsC_6H_3(CH_3)NHCOCH_3$, produced by acetylating the corresponding arsonic acid with acetic anhydride and a little concentrated sulfuric acid, crystallizes in colorless prisms more soluble in water than the 3-methyl isomer. It darkens at 240°, but is not entirely decomposed at 350°.[959]

4-Acetylamino-3-methylphenylarsonic acid separates as slender needles or acicular prisms on reacting sodium-4-amino-3-methylphenylarsonate with acetic anhydride. It decomposes at 306° without previous melting, is insoluble in water, alcohol, ether, or dilute acids, but dissolves readily in methyl alcohol (Wellcome), or alkalis.[960, 959] Its monosodium salt (*"Orsudan"*) crystallizes from 50 per cent alcohol with 5, and from water with $7H_2O$.[944]

4-Acetylamino-2,5-dimethylphenylarsonic acid,

$$H_2O_3AsC_6H_2(CH_3)_2NHCOCH_3,$$

crystallizes from water in prisms, turning brown at 240° and decomposing with frothing at 278°.[959]

3-Carbethoxyaminophenylarsonic acid, $H_2O_3AsC_6H_4NHCOOC_2H_5$, is obtained as beautiful needles melting with decomposition at 180°, upon adding ethylchlorocarbonate to a sodium carbonate solution of m-arsanilic acid at 0-5°, and finally acidifying.[724]

6-Oxalylamino-3-methylphenylarsonic acid, $C_6H_3\begin{cases} AsO(OH)_2 \\ CH_3 \\ NHCOCOOH \end{cases}$,

is made from the sodium salt of the corresponding arsonic acid and oxalic acid by heating at 130-40° until all the water is removed, then further at 160° until pulverulent, and finally acidifying with hydrochloric acid. The anhydrous product is sparingly soluble in hot alcohol, ethyl acetate or acetone, more readily in hot water, and easily in 50 per cent acetic acid, from which it crystallizes in elongated rhombic prisms. On nitration with nitric-sulfuric acid, 5-nitro-6-amino-3-methylphenylarsonic acid results.[961]

o,o′-Diarsono-oxanilide [N,N′-Oxalylbis-o-arsanilic acid], [2-Aminophenylarsonic acid oxanilide], $\begin{matrix} CO.HNC_6H_4AsO_3H_2 \\ | \\ CO.HNC_6H_4AsO_3H_2 \end{matrix}$, is obtained when 2,5-diaminophenylarsonic acid oxanilide is diazotized, and then warmed with alcohol and copper bronze at 55-60°. Leaflets with a silvery luster.[935]

4-Carbamido-3-methylphenylarsonic acid,

$$H_2O_3AsC_6H_3\begin{cases} CH_3 \\ NHCONH_2 \end{cases},$$

is prepared by acidifying an aqueous solution of sodium 4-amino-3-methylphenylarsonic acid and potassium cyanate with acetic acid, and saturating, after 24 hours, with hydrochloric acid.[962]

N-4-Allylthiocarbamido-2-methylphenylarsonic acid,

$$H_2O_3AsC_6H_3(CH_3)NHCSNHC_3H_5,$$

derived from 4-amino-2-methylphenylarsonic acid and allylthiocarbimide in methyl alcohol, decomposes at 170°.[963]

2-Methylphenyl-(4-arsonic acid) glycine,

$$H_2O_3AsC_6H_3(CH_3)NHCH_2COOH,$$

from sodium 4-amino-3-methylphenylarsonate and chloroacetic acid, melts with decomposition at 220°, is very sparingly soluble in hydrochloric acid, but readily in hot water, alkalis or alcohol.[520]

N-(Phenyl-2-arsonic acid) glycineamide,

$$H_2O_3AsC_6H_4NHCH_2CONH_2,$$

is formed when o-arsanilic acid, dissolved in N-sodium hydroxide solution, is treated with chloroacetamide. Unlike the meta and para isomers, this acid is not displaced completely from its salts by so weak an acid as acetic. The substance consists of long, thin, narrow plates soluble in hot 50 per cent alcohol or boiling water, sparingly in hot methyl or ethyl alcohol and decomposing on rapid heating at 198-9°.[964]

N-(Phenyl-3-arsonic acid) glycineamide results on boiling m-arsanilic acid and chloroacetamide in N-sodium hydroxide solution. Prismatic needles, readily soluble in hot glacial acetic acid, methyl or ethyl alcohol or warm water, quite soluble in cold water, but practically insoluble in hot acetone. When rapidly heated to 170° and then slowly, the substance melts at 175-7° to a liquid filled with bubbles.[964]

N-(2-Methylphenyl-4-arsonic acid) glycineamide,

$$H_2O_3AsC_6H_3(CH_3)NHCH_2CONH_2,$$

from 4-amino-3-methylphenylarsonic acid and chloroacetamide. It forms aggregates of glistening platelets, which decompose at about 283° with previous darkening; are sparingly soluble in boiling water, but more readily so in boiling 50 per cent alcohol.[965]

N-(2-Methylphenyl-5-arsonic acid) glycineamide, similarly prepared from 3-amino-4-methylphenylarsonic acid, consists of delicate interlaced needles which do not melt below 285°, and are soluble in methyl alcohol, warm water, ethyl alcohol or acetic acid.[965]

N-(3-Methylphenyl-4-arsonic acid) glycineamide, similarly obtained from 4-amino-2-methylphenylarsonic acid, is soluble in boiling 50 per cent alcohol or water, separating from the latter in lustrous, diamond-shaped platelets, which melt at 203-5° with gas evolution.[965]

N-(2,5-Dimethylphenyl-4-arsonic acid) glycineamide,

$$H_2O_3AsC_6H_2(CH_3)_2NHCH_2CONH_2.$$

From 4-amino-2,5-dimethylphenylarsonic acid by boiling with chloroacetamide in alkaline solution, and acidifying with hydrochloric acid.

The compound consists of aggregates of slightly brownish plates and prisms sparingly soluble in cold water, acetic acid or 50 per cent alcohol, but more easily on boiling. On rapid heating it melts and decomposes at 236-7° with preliminary darkening and softening.[965]

N-(Phenyl-3-arsonic acid)glycine methylamide,

$$H_2O_3AsC_6H_4NHCH_2CONHCH_3,$$

is formed on boiling chloroacetylmethylamine with a solution of sodium-m-arsanilate. It exists as microscopic needles or platelets readily soluble in hot water or 50 per cent alcohol but sparingly in cold. When rapidly heated it darkens and melts at 193-4.5° with gas evolution.[964]

N-(Phenyl-2-arsonic acid)glycineanilide,

$$H_2O_3AsC_6H_4NHCH_2CONHC_6H_5,$$

from sodium-o-arsanilate and chloroacetanilide, crystallizes in radiating masses of minute prisms with $1H_2O$. The anhydrous substance softens at 158°, melts at 160-3° with slow gas evolution; dissolves readily in boiling 50 per cent alcohol, warm acetic acid or cold methyl alcohol, sparingly in cold alcohol or acetic acid, and very difficultly in boiling water.[966]

N-(Phenyl-3-arsonic acid)glycineanilide is obtained from m-arsanilic acid and chloroacetanilide in the form of rosets of minute, cream-colored prisms, containing solvent of crystallization. On rapid heating it decomposes at 217-18° with preliminary darkening and softening. It is readily soluble in hot acetic acid or 50 per cent alcohol, fairly soluble in cold 95 per cent alcohol, and sparingly in hot water.[967]

N-(Phenyl-2-arsonic acid)glycyl-2'-aminophenol,

$$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4OH.$$

From o-arsanilic acid and o-chloroacetylaminophenol by boiling in sodium hydroxide solution for one-half hour. It exists as glistening needles containing $\frac{1}{2}H_2O$, and, when anhydrous melts with decomposition at 151-3°. From hot water, in which it is but sparingly soluble, it separates on cooling as long, silky needles fairly readily soluble in cold methyl or ethyl alcohol, and more so in hot 50 per cent alcohol. An alkaline solution couples readily with diazotized sulfanilic acid.[966]

N-(Phenyl-2-arsonic acid)glycyl-3'-aminophenol, prepared in like manner from m-chloroacetylaminophenol, consists of bundles of pink microscopic platelets which, when air-dried, contain approximately $2H_2O$ and melt at 103-5°. The anhydrous substance softens at about 125-30°, and melts with decomposition at about 180°. It is readily soluble in

methyl or ethyl alcohol, acetic acid or hot water, and in alkaline solution couples readily with diazotized sulfanilic acid.[968]

N-(Phenyl-2-arsonic acid)glycyl-4'-aminophenol. — Equimolecular proportions of o-arsanilic acid and p-chloroacetylaminophenol yield a heavy powder consisting of short, colorless, microscopic platelets. When rapidly heated the acid darkens and then melts with decomposition at 208-9°. It is easily soluble in boiling methyl or 50 per cent ethyl alcohol, but very sparingly in boiling water.[968]

N-(Phenyl-3-arsonic acid)glycyl-2'-aminophenol. — Almost colorless, flat, microscopic needles from m-arsanilic acid and o-chloroacetylaminophenol. When rapidly heated to 185°, then slowly, it darkens and softens, finally melting with decomposition at 190-2°. It is sparingly soluble in cold water, 50 per cent or 95 per cent alcohol, more easily on warming, and is readily soluble in cold methyl alcohol or boiling acetic acid. A solution of the acid in strong ammonium acetate slowly deposits the ammonium salt as minute needles. Although hydrochloric acid reprecipitates the acid from its salts as a gummy mass, an excess of acetic acid causes no immediate precipitation, but on long standing the arsonic acid separates slowly and incompletely as crusts of broad, microscopic needles.[967]

N-(Phenol-3-arsonic acid)glycyl-3'-aminophenol, prepared from m-arsanilic acid and m-chloroacetylaminophenol, is a light purple powder consisting of minute, irregular platelets and flat needles containing about $1\frac{1}{2}H_2O$. On rapidly heating to 150° the anhydrous substance sinters to a tar which decomposes at 180-90°. In the cold it dissolves more readily in methyl alcohol than in the other solvents, is fairly easily soluble in hot water, alcohol or acetic acid, and practically insoluble in acetone, benzene or ether.[969]

N-(Phenyl-3-arsonic acid)glycyl-4'-aminophenol.—From m-arsanilic acid and p-chloroacetylaminophenol. On rapidly chilling its hot concentrated aqueous solution it separates as a milky emulsion which then very slowly crystallizes, partly as a hydrate; on slow cooling, however, anhydrous microscopic platelets are obtained. It decomposes at 180° with previous sintering and darkening, is easily soluble in boiling water or hot ethyl alcohol, appreciably so in methyl alcohol, but sparingly in cold water or hot acetone. It dissolves in warm, dilute hydrochloric acid, but on the addition of more concentrated acid the hydrochloride gradually separates.[970]

N-(2-Methylphenyl-4-arsonic acid)glycyl-3'-aminophenol,

$$H_2O_3AsC_6H_3(CH_3)NHCH_2CONHC_6H_4OH,$$

is obtained from sodium 4-amino-2-methylphenylarsonate and m-chloroacetylaminophenol as long, flat, microscopic needles practically insoluble

in boiling water, appreciably soluble in hot 50 per cent alcohol, and decomposing at 285° with preliminary darkening. Its alkaline solution couples readily with diazotized sulfanilic acid.[970]

N-(2-Methylphenyl-4-arsonic acid)glycyl-4′-aminophenol, prepared like the preceding isomer, exists as microscopic, spindle-shaped needles, very sparingly soluble in boiling water, slightly more so in hot 50 per cent alcohol and decomposing at 232-3° with preliminary darkening.[970]

N-(3-Methylphenyl-4-arsonic acid)glycyl-3′-aminophenol is prepared like the two preceding isomers, starting with 4-amino-2-methylphenylarsonic acid. Aggregates of spindle-shaped microcrystals very sparingly soluble in boiling water or alcohol, more readily in hot 50 per cent alcohol, and decomposing at 232-5° with preliminary softening and darkening. Its alkaline solution couples readily with diazotized sulfanilic acid.[971]

N-(2-Carboxyphenyl-4-arsonic acid)glycyl-3′-aminophenol,

$$HOOC(H_2O_3As)C_6H_3NHCH_2CONHC_6H_4OH,$$

results upon boiling for one hour a mixture of alkaline 4-amino-3-carboxyphenylarsonic acid, acetic acid and m-chloroacetylaminophenol, the compound finally separating as thin, minute platelets containing one molecule of water of crystallization. The substance is practically insoluble in boiling water, somewhat soluble in hot alcohol or 50 per cent alcohol, and fairly readily in boiling methyl alcohol or glacial acetic acid. When rapidly heated the anhydrous acid darkens and swells, then decomposes at 204-7°. Its alkaline solution couples readily with diazotized sulfanilic acid.[971]

N-(Phenyl-2-arsonic acid)glycineureide,

$$H_2O_3AsC_6H_4NHCH_2CONHCONH_2,$$

precipitates upon boiling an alkaline solution of o-arsanilic acid with chloroacetylurea. Minute, delicate needles, almost insoluble in the usual neutral solvents, and melting with decomposition at 231-2° with preliminary softening and yellowing.[972]

N-(Phenyl-3-arsonic acid)glycineureide, from m-arsanilic acid like the corresponding ortho compound, separates as colorless microscopic needles frequently grouped in bundles. It is soluble in boiling water or 50 per cent alcohol crystallizing from the former in rosets of minute needles decomposing at 208-9° with preliminary softening.[973]

N-(3-Methylphenyl-4-arsonic acid)glycineureide,

$$H_2O_3AsC_6H_3(CH_3)NHCH_2CONHCONH_2.$$

Delicate needles from 4-amino-3-methylphenylarsonic acid and chloroacetylurea in alkaline solution. The substance is sparingly soluble in

boiling water or 50 per cent alcohol, and decomposes on rapid heating at about 235°. The sodium salt, containing $2H_2O$, separates as glistening plates on adding alcohol to the carefully neutralized acid.[973]

N-(2-Hydroxyphenyl-5-arsonic acid)glycineureide,

$$H_2O_3AsC_6H_3(OH)NHCH_2CONHCONH_2.$$

Produced as above from 3-amino-4-hydroxyphenylarsonic acid and chloroacetylurea. Flat, minute, almost colorless, glistening needles containing between one and one and one-half molecules of water or crystallization. When anhydrous it decomposes at 203-5°.[974]

N-(Phenyl-2-arsonic acid)glycinemethylureide,

$$H_2O_3AsC_6H_4NHCH_2CONHCONHCH_3,$$

results on boiling an alkaline solution of o-arsanilic acid with α-chloroacetyl-β-methylurea until almost solid, and finally heating on a water bath. It forms balls of minute needles which readily dissolve in boiling acetic acid, sparingly in boiling water, alcohol or methyl alcohol, and decompose at 218° with slight preliminary softening and darkening.[972]

N-(Phenyl-3-arsonic acid)glycinemethylureide.—From m-arsanilic acid and α-chloroacetyl-β-methylurea. It melts with decomposition at 213-3.5°; is sparingly soluble in boiling water or 50 per cent alcohol, depositing from the former in rosets of delicate needles.[973]

N-(3-Methylphenyl-4-arsonic acid)glycine-methylureide,

$$H_2O_3AsC_6H_3(CH_3)NHCH_2CONHCONHCH_3,$$

results on boiling sodium-4-amino-3-methylphenylarsonate with α-chloroacetyl-β-methylurea for one hour. It is sparingly soluble in hot water and readily in boiling 50 per cent alcohol, separating from the former as hair-like needles, and from the latter as radiating masses of minute needles. When rapidly heated it decomposes at 218-9°.[974]

4-Dimethylamino-2-methylphenylarsonic acid,

$$(CH_3)_2NC_6H_3(CH_3)AsO(OH)_2,$$

prepared by oxidizing the corresponding arsineoxide, decomposes at 225°.[975]

4-Dimethylamino-3-methylphenylarsonic acid results on oxidation of the corresponding arsineoxide with an aqueous suspension of red mercuric oxide. It forms gray leaflets, m. p. 245°.[976]

4-Dimethylamino-2,5-dimethylphenylarsonic acid,

$$(CH_3)_2NC_6H_2(CH_3)_2AsO_3H_2,$$

decomposes at 216°.[977]

2-Dimethylaminonaphthylarsonic acid, $(CH_3)_2NC_{10}H_6AsO(OH)_2$, decomposes at 309°.[978]

4-Dimethylaminonaphthylarsonic acid decomposes at 192°.[979]

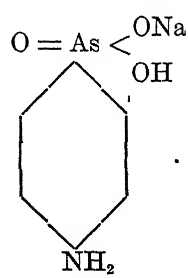
9. **p-Arsanilic Acid and Its Derivatives.**—*4-Aminophenylarsonic Acid* (p-Arsanilic Acid).

In 1863 there appeared a publication by Béchamp[27] in which he described a colorless product obtained by heating aniline arsenate at 190-200°. He assumed it to be an acidic anilide of the formula $C_{12}H_8AsO_6N$, which in the light of subsequent developments in organic chemistry, would be represented by the constitutional formula, $C_6H_5.NH.As(OH)_2$. Béchamp also noted that his new compound behaved like a monobasic acid which was not hydrolyzed by aqueous caustic potash and formed well-defined sodium, potassium, barium and silver salts. The above formula was accepted as correct for the next 40 years, when an arsenical by the name of "Atoxyl" began to find application in therapeutics, and because of its valuable spirocheticidal properties became the subject of numerous investigations. In 1907 Ehrlich[980] claimed this drug to be identical with the monosodium salt of Béchamp's acid, except that it contained four instead of five molecules of water of crystallization; Fourneau[981] regarded it as the monosodium salt of the anilide of ortho arsenic acid containing $2H_2O$, whose formula was

$$C_6H_5.NH.AsO\begin{matrix} \diagup ONa \\ \diagdown OH \end{matrix} .2H_2O,$$

while a sample of the same compound investigated by Moore, Nierenstein and Todd[982] was found to contain $3H_2O$.

It remained for Ehrlich and Bertheim to prove the real structure of atoxyl, which they declared to be the monosodium salt of p-aminophenylarsonic acid whose constitution may be expressed by the graphic formula:



As conclusive evidence of their claims, they offered the following considerations:

1. On boiling an aqueous solution of the compound with alkalis, concentrated hydrochloric or 30 per cent sulfuric acid no aniline is split off, decomposition occurring only on heating the aqueous solution above its boiling point under pressure or by fusion with caustic alkalis. This is contrary to the behavior of ordinary anilides which are readily hydrolyzed.

2. The presence of a primary amino group can be demonstrated by the fact that it behaves like an aromatic amine, without losing its arsenic. Thus, it may be readily diazotized, and the resulting diazo compound coupled with amines or phenols to form azo dyes; it can be acetylated; and it yields an intensely red condensation product with sodium β-naphthoquinonesulfonate.

3. Like typical arsonic acids, its ammoniacal solution yields no precipitate with magnesia mixture or calcium chloride in the cold, but only at boiling temperature.

4. The relative positions of the arsonic acid and amino groups may be demonstrated upon replacing the first with iodine by means of hydriodic acid, when p-iodoaniline is obtained.

They also explained the reactions involved in preparing p-aminophenylarsonic acid from aniline and arsenic acid, saying that aniline arsenate is first formed, which upon further heating undergoes a molecular rearrangement, the arsonic acid radical entering the para position:

$$C_6H_5NH_2 + H_3AsO_4 \longrightarrow C_6H_5NH_2.H_3AsO_4 \longrightarrow$$

$$C_6H_4\begin{cases} AsO(OH)_2 \\ NH_2 \end{cases} + H_2O.$$

On account of the similarity of this reaction with that occurring in the preparation of sulfanilic acid, they named the above arsonic acid "Arsanilic Acid." [983]

4-Aminophenylarsonic acid has served as the starting point for the preparation of a great number of new arsenicals. Thus, the hydrogen of the amino group has been replaced by various acyl and alkyl groups. In addition to the simple substituents, products have been obtained by condensing p-arsanilic acid or its sodium salt with chloro- fatty acids, acid amides, or chloroacylated alkyl- or arylamines; with α-chloroacetyl ureas and various β-alkyl or aryl derivatives of the same, $ClCH_2CO.HN.CO.NHR$; with aromatic chloroacetylamino compounds, $ClCH_2CONHR$; with α-phenylchloroacetylamines, $\begin{matrix} Cl \\ \diagdown \\ CH.CO.NHR', \\ \diagup \\ C_6H_5 \end{matrix}$

and with chloroarylhalides containing the halogen in the side chain. Furthermore, it can be chloroacetylated, and the halogen of the acetyl group replaced by amino derivatives, yielding compounds of the type

$$C_6H_4\left\langle\begin{array}{l}AsO_3H_2\\ NH.COCH_2NHR\end{array}\right.$$

. One of the most interesting of these numerous derivatives is N-phenylglycineamide-p-arsonic acid ("Tryparsamide"),

$$C_6H_4\left\langle\begin{array}{l}AsO_3H_2\\ NH.CH_2CONH_2\end{array}\right.$$

, which has been the subject of considerable investigation in the treatment of trypanosome and spirochete infections.

p-Arsanilic acid can be readily diazotized and the resulting diazonium salt converted into well-defined diazo amino compounds by coupling with dialkyl or simple aryl amines, aminobenzoic acids, aryl glycines or aminophenoxyacetic acids. The coupling with secondary aliphatic- or simple arylamines proceeds smoothly in solutions which are neutral or acid with a weak acid like acetic. The aromatic amino acids usually couple smoothly, while the simpler aminobenzoic acids yield diazo compounds under carefully controlled conditions by using the amino acid itself as the coupler and isolating the products as the monosodium salts. In the case of aminophenoxyacetic acids, the coupling either does not proceed entirely in the desired sense, or the resulting diazo-amino compounds possess properties which render their isolation difficult. In such cases coupling can be effected with amino acid esters, yielding the diazo-amino esters, which can be readily hydrolyzed with caustic alkali to the diazo-amino acids.

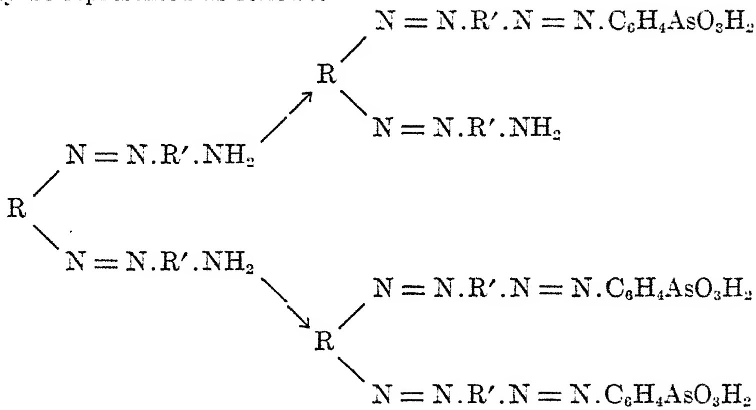
The diazonium salt of p-arsanilic acid may also be coupled with various azo components yielding azo dyes. Among the coupling agents employed have been aromatic amines, phenols, methoxynaphthylamines, substituted aminobenzoic acids, aromatic glycines, aromatic N-methyl sulfonic acids and substituted phenoxyacetic acids. The reaction between the diazotized arsanilic acid and the coupler usually proceeds smoothly, but the isolation and purification of the resulting dyes often present considerable difficulty, and much experimentation is necessary in each case to discover the best conditions for coupling and the best method for isolating the compound—whether as the free acid, the mono- or disodium salt. The monosodium salts are generally sparingly soluble in water, while the disodium compounds are readily so. The latter generally yield precipitates with salts of the heavier metals when in very dilute solutions, while their behavior with the salts of the alkaline earths is varied.

The azo dyes containing a free amino group may be further combined with another mole of 4-diazophenylarsonic acid in alkaline solution, yielding a disazo dye of the type,

$$H_2O_3As.C_6H_4.N = N.R.N = N.C_6H_4AsO_3H_2.$$

Similar products may be obtained by diazotizing an aromatic diamine with two moles of sodium nitrite and coupling with two moles of p-arsanilic acid, or by condensing 4-nitrosophenylarsonic acid (2 moles) with a diamine.

By diazotizing various para diamines, coupling with 2 moles of doubly coupling components and combining these intermediate dyes with one or two moles of 4-diazophenylarsonic acid, there are obtained tris- and tetraazo arsenical dyes respectively. The procedure involved may be represented as follows:

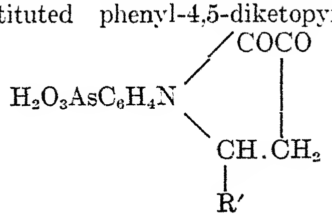


where R′ represents a doubly linking component such as H acid, 1-amino-8-naphthol-4-sulfonic acid (S acid), or 1,8-dihydroxynaphthalene-3,6-disulfonic acid (chromotropic acid).

Finally, p-arsanilic acid in aqueous or aqueous alcoholic solution, in the presence of a condensing agent may be condensed with aldehydes, especially aromatic, to azomethine compounds of the formula

$$H_2O_3As.C_6H_4.N = CH.R'.$$

If a mineral acid be employed as the dihydrating agent, the product obtained is a salt. By condensing p-arsanilic acid with aromatic aldehydes and pyruvic acid in alcoholic medium, there are formed 1-(4′-arsonophenyl)-2-phenyl or substituted phenyl-4,5-diketopyrrolidines, corresponding to the formula



(where

R′ = a phenyl or substituted phenyl radical. In this manner products with benzaldehyde, 4-chlorobenzaldehyde, salicylaldehyde methyl ether, anisaldehyde, and piperonal have been obtained.

With mercuric acetate in aqueous solution at 100°, sodium-p-arsanilate yields a mixture of mono- and dihydroxymercuri-4-aminophenylarsonic acids, the mercury entering the nucleus.

4-Aminophenylarsonic acid (*p-Arsanilic acid*), first obtained by Béchamp[27] upon heating aniline arsenate at 190-200°, may now be prepared in a number of ways. The following unpublished method, developed by Raiziss and Gavron, has been found suitable for the preparation of the pure arsonic acid on both laboratory and factory scales. Crude arsenic acid (containing 70-75% of H_3AsO_4) is concentrated and simultaneously freed of oxides of nitrogen and other volatile impurities by warming on a water bath in vacuo, 4.3 kg. of the resulting liquid (containing 80-82% of H_3AsO_4) is then thoroughly mixed with 2.5 l. of pure aniline (98-100°) in an enamel pot (diameter = 23 cm.; depth = 19 cm.), and the temperature gradually raised to 160° in an oil bath, requiring 3.5 hours. The melt is then maintained at the above temperature for one-half hour, when it is first gradually diluted with 4 l. of water, then rendered alkaline with 2.75 l. of 40% aqueous caustic soda, and finally allowed to settle for one-half hour. The upper layer is then distilled with steam to recover the unused aniline, while the lower layer, containing the sodium arsanilate, is mixed with 175 g. of "Filter Cell," allowed to stand at ordinary temperature for 14 hours, filtered, and the filtrate rendered slightly acid to congo-paper with hydrochloric acid. The crude product is then purified by dissolving in aqueous caustic soda, mixing with 350 g. of animal charcoal for four hours at ordinary temperature, filtering and acidifying as before.

According to another method a mixture of pure dry arsenic acid (47 g.) and aniline (152 c.c.) is heated in a paraffine-bath at 150-160° for 12 hours. The liquid is then cooled, treated with 60 c.c. of 6N-sodium hydroxide solution, and the aniline which separates out removed by means of a separatory funnel. The remaining sodium arsanilate solution is now clarified with 15-20 gms. of infusorial earth, and the filtrate acidified with 50 c.c. of 6 N-hydrochloric acid, whereupon the arsanilic acid generally crystallizes on cooling, although it is frequently necessary to stir the filtrate on account of its tendency to become supersaturated.[984]

A modification of this method consists in adding practically 100% arsenic acid (obtained by heating 1 liter of 76% arsenic acid in an oil bath at 120-40° for 12-15 hours) to 1400 c.c. of constantly stirred dry aniline previously cooled to 0°, forming a salt of the approximate composition, $(C_6H_5NH_2)_3(H_3AsO_4)_2$. A portion of the resulting mass (200 g.) is ground, thoroughly mixed, and then heated with stirring on an oil bath at 160° until all is melted, when a reflux condenser is

attached, the liquid further heated for 1.5 hours at 160°-70° and for another hour at 180-185°. The melt is then treated with 225 c.c. of 6 N-caustic soda and 225 c.c. of water, and then worked up as before.[985]

By a third method 4.8 gms. of 4-nitrophenylarsonic acid is dissolved in 150 c.c. of water to which either 20 c.c. of 2N-caustic soda or 5.6 gms. sodium acetate has been added, and reduced with hydrogen gas under a pressure of 2-3 atmospheres in the presence of about 0.1 g. of precipitated palladous hydroxide with constant shaking. When reduction is complete the palladium is filtered off, the solution concentrated on a water-bath to about 30 c.c., and the product precipitated by the addition of dilute hydrochloric acid.[901]

Finally the compound may be obtained by reducing the corresponding nitro acid with ferrous hydroxide,[917] or by hydrolyzing acetyl-p-arsanilic acid.[986]

The crude acid may be purified either by recrystallization from hot water or through its sodium salt. In the latter method the acid is dissolved in sufficient aqueous caustic soda to render the resulting solution faintly alkaline, decolorized with animal charcoal, and precipitated in alcohol. The sodium salt ("Atoxyl") crystallizes out, and is converted into the free acid by transposing with dilute hydrochloric acid. It forms white needles, readily soluble in excess of dilute mineral acids, alkalis, methyl alcohol or hot water, less so in ethyl alcohol or glacial acetic acid, sparingly in cold water, and practically insoluble in ether or acetone. At 150° it loses one molecule of water, but does not decompose below 300°. By boiling its aqueous solution with alkalis, concentrated hydrochloric or 30% sulfuric acid no aniline is split off, decomposition being only obtained either by heating the aqueous solution above its boiling point under pressure, or by fusion with caustic alkalis. It forms condensation products with β-naphthoquinonesulfonic acid or aromatic aldehydes; it may also be acetylated or diazotized, the diazo solution yielding azo dyes upon coupling with amines or phenols. As a typical arsonic acid its arsenic may be replaced by iodine upon warming with hydriodic acid, and its ammoniacal solution yields a precipitate with magnesium salts only upon boiling. It may be quantitatively determined by means of sodium nitrite.

Its hydrochloride is readily soluble in methyl or ethyl alcohol from which it may be precipitated by ether.[987] The monosodium salt (*"Atoxyl," "Arsamin," "Soamin," "Natrium Arsanilicum"*) crystallizes with two to six molecules of water depending on the solvent employed. It is a white crystalline compound readily soluble in water or methyl alcohol, but practically insoluble in ethyl alcohol.[988] When its neutral solution is treated with auric chloride a deep red liquid is obtained, from which the reduced gold completely separates on standing as a black powder. In alkaline solution, however, a stable, ruby-red colloidal gold solution results.[989] On adding atoxyl to aqueous sodium formaldehyde

sulfoxylate at 70°, there is first formed a solution of sodium arsanili methylenesulfoxylate, which upon further treatment with magnesia n ture is precipitated as the sodium-magnesium salt of arsanilidometl enesulfoxylic acid, $MgO_3AsC_6H_4.NHCH_2OSONa.2H_2O$, soluble in di acids and reducing indigo carmine upon warming.[990] Atoxyl also fo an addition product with hydroxymethylenecamphor upon warming intimate mixture of the components at 110°[991]

Upon adding successively molybdenum trioxide and guanidin chloride to a hot aqueous solution of atoxyl, there is obtained a mixt of yellow needles and pale yellow leaflets which may be separated recrystallization from water.[992] The less soluble, pale yellow leaf correspond to the formula, $(CN_3H_6)_2\left[As\begin{matrix}C_6H_4.NH_2\\(MoO_4)_3\end{matrix}\right].5H_2O$, while yellow needles have the formula,

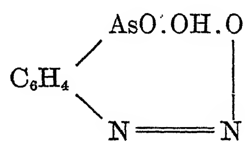
$$(CN_3H_6)_5H_5\left[\underbrace{As\begin{matrix}C_6H_4.NH_2\\(MoO_4)_4\end{matrix}\qquad\begin{matrix}H_2N.C_6H_4\\(MoO_4)_4\end{matrix}As}_{MoO_4}\right].$$

The quinine salt of p-arsanilic acid, precipitated upon mixing so tions of atoxyl and soluble quinine salts, forms white needles, m. 202°, soluble in hot alcohol or dilute mineral acids, sparingly in glycerine or water, and insoluble in ether, ligroin, benzene or car tetrachloride. The cinchonine salt, similarly prepared, forms mic scopic prisms decomposing at 180°, soluble in dilute mineral acids, c methyl or hot ethyl alcohol, but insoluble in alkalis, water, ether, chlc form or carbon tetrachloride.[993] The mercuric salt,

$$(H_2N.C_6H_4AsO.OH.O)_2Hg,$$

is known as *"Asiphyl"* or *"Aspirochyl,"* and is made either by the act of two molecular proportions of arsanilic acid upon one of merc oxide or by the interaction of atoxyl with mercuric chloride. It i white powder, readily soluble in sodium chloride solution, sparingly water, and decomposed by alkalis forming mercuric oxide.[994, 995] When equimolar proportions of arsanilic acid and mercuric oxide reac the presence of two mols. of alkali, a salt, $H_2N.C_6H_4AsO.OH.OHg($ is formed, having the same properties as the preceding compound.[9

4-Diazophenylarsonic acid (*Benzenediazonium-4-arsonate*),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prepared by diazotizing p-arsanilic acid in the ordinary way, may be precipitated as a white double salt with phosphotungstic acid. It exhibits the characteristic properties of diazonium salts: when warmed with dilute sulfuric acid it is converted into 4-hydroxyphenylarsonic acid; it yields 4-chlorophenylarsonic acid upon treatment with copper powder and hydrochloric acid, and also couples with phenols and other reactive bases such as m-toluylenediamine.[997]

Unless otherwise specified the following diazo-amino compounds have been prepared by coupling 4-diazophenylarsonic acid with various amines: [998]

Dimethylamine.—Orange spears from alcohol, intumescing at 182°, soluble in methyl alcohol, very difficultly in cold alcohol, and decomposing in boiling water with evolution of nitrogen. Its sodium salt crystallizes in lustrous, salmon-colored platelets readily soluble in water.

Diethylamine.—Cream-colored needles which when anhydrous gradually soften and darken above 120°, finally decomposing at 195-200°. It is readily soluble in methyl alcohol or acetic acid. The sodium salt crystallizes in rosets of somewhat deliquescent cream-colored needles.

Piperidine.—Pale drab spherules and rosets of platelets, m. p. 162-3° with effervescence; soluble in methyl or ethyl alcohol. Its sodium salt separates from 85% alcohol in platelets.

Hexamethylene tetramine.—Upon coupling in sodium acetate solution formaldehyde is split off, the sodium salt of bis(4-diazophenylarsonic acid)-pentamethylene tetramine crystallizing with $6H_2O$ in lustrous colorless platelets. The free acid forms platelets decomposing in boiling water, and practically insoluble in neutral solvents.

Aniline.—Yellow needles, m. p. 112-3° with decomposition, readily soluble in hot methyl or ethyl alcohol and decomposing in boiling water. The sodium salt crystallizes in orange platelets and flat needles readily soluble in water.

Methylaniline.—Orange-brown aggregates of minute needles effervescing at 160-2°, and soluble in dilute acid. Sodium salt—lustrous orange platelets.

p-Toluidine.—Pale yellow needles intumescing at 130-2° and soluble in hot alcohol. Sodium salt—lustrous yellow leaflets.

4-Chloroaniline.—Hexagonal platelets intumescing at 177°; practically insoluble in neutral solvents. Sodium salt—almost colorless platelets from 50% alcohol.

o-Anisidine.—Flat microscopic needles intumescing at 95-9°. Sodium salt—brown platelets readily soluble in water.

p-Anisidine.—Pale brown leaflets soluble in methyl alcohol, decomposing at 110°, and intumescing at 116-19° when anhydrous. Sodium salt—rosets of pale brown leaflets from 50% alcohol.

4-Aminoacetanilide.—Lustrous hexagonal platelets decomposing at

165-70° when anhydrous. Sodium salt—microscopic leaflets from 50% alcohol.

4-Aminophenylbenzoate.—Prepared by diazotizing 4-aminophenylbenzoate and coupling with p-arsanilic acid. It crystallizes from methyl alcohol-water in yellow leaflets decomposing at 155-8°, and is practically insoluble in neutral solvents except hot methyl or ethyl alcohol.

4-Aminophenol.—From the preceding compound by dissolving in four equivalents of 2N-sodium hydroxide, allowing to stand for 15 minutes at room temperature, saturating with sodium acetate, and finally neutralizing at low temperature with acetic acid. The sodium salt gradually separates, and may be obtained from 85% alcohol in rosets of yellow needles. The free acid is too unstable to be isolated.

4-Aminoacetophenone.—Bright yellow needles intumescing at 177-8°, soluble in boiling methyl alcohol. Sodium salt—brownish-yellow rosets of flat needles from 85% alcohol.

2-Aminobenzoic acid.—Yellow needles intumescing at 160°, soluble in hot methyl or ethyl alcohol. Its monosodium salt consists of flat yellow needles difficultly soluble in cold water, while the disodium salt crystallizes from 85% alcohol in long, flat, yellow needles easily soluble in water.

3-Aminobenzoic acid.—Buff-colored microcrystalline rosets intumescing at 141°, and soluble in hot methyl or ethyl alcohol. The monosodium salt is a cream-colored microcrystalline, anhydrous substance. The disodium salt separates from 70% alcohol in long, thin, pale yellow needles.

4-Aminobenzoic acid.—Microscopic needles. From 50% alcohol the monosodium salt deposits in microscopic needles very sparingly soluble in cold water.

3-Amino-6-methoxybenzoic methyl ester.—Buff-colored aggregates of platelets melting at 90-5° with gas evolution, and soluble in methyl or ethyl alcohol.

3-Amino-6-methoxybenzoic acid.—Obtained as the disodium salt from the preceding ester by warming with alcoholic caustic soda. It separates from 70% alcohol in rosets of pale brownish-yellow hygroscopic needles. The free acid forms rosets of yellow microscopic needles decomposing at 140° when anyhdrous.

3-Aminoanisic methyl ester.—Glistening yellow needles from 50% alcohol, decomposing at 150°, and readily soluble in methyl alcohol.

3-Aminoanisic acid.—Obtained as the disodium salt either by saponifying the preceding compound, or by adding sodium-3-aminoanisate to a neutralized diazo solution of p-arsanilic acid and precipitating with an equal volume of absolute alcohol. It separates in balls of yellow needles from 70% alcohol. The free acid forms aggregates of yellow microscopic needles intumescing at 150-5° when anhydrous, and is difficultly soluble in hot methyl alcohol.

6-Aminopiperonylic methyl ester.—Almost colorless needles remaining undecomposed below 280°, and practically insoluble in neutral solvents. When saponified it does not yield the pure sodium salt, so that the free acid cannot be obtained.

4-Aminocinnamic ethyl ester.—Obtained as the sodium salt by diazotizing the amino ester, coupling with p-arsanilic acid, and adding saturated sodium acetate solution. It forms bright yellow needles from 70% alcohol and is sparingly soluble in cold water. The free acid consists of aggregates of yellow needles decomposing at 155-60°.

4-Aminocinnamic acid.—The disodium salt, obtained by saponifying the ethyl ester, crystallizes from 70% alcohol in yellow needles readily soluble in water. The acid forms yellow needles decomposing at 155-60° when anhydrous, and appreciably soluble in boiling methyl alcohol.

4-Aminophenylarsonic acid.—Pale yellow needles from 95% alcohol, intumescing at 154°. Its monosodium salt consists of yellow, lustrous platelets, and the disodium salt of yellow needles, both readily soluble in water.

Phenylglycine.—Has not been obtained free of the corresponding azo dye. The monosodium salt, brownish yellow needles, is sparingly soluble in cold water.

p-Tolylglycine.—Flat needles intumescing at 148-9° and appreciably soluble in alcohol. Monosodium salt—tan-colored needles difficultly soluble in cold water.

Benzylglycine.—Practically colorless, lustrous needles and prisms intumescing at 155-60°, and readily soluble in methyl alcohol.

4-Methoxyphenylglycine ethyl ester.—Cannot be obtained crystalline. Sodium salt—yellowish-brown leaflets and needles easily soluble in water.

4-Methoxyphenylglycine.—Cannot be obtained crystalline. The monosodium salt may be prepared either by saponifying the corresponding ethyl ester, or by coupling 4-diazophenylarsonic acid with the sodium salt of 4-methoxyphenylglycine. It crystallizes in yellow platelets readily soluble in warm water but sparingly in cold.

4-Ethoxyphenylglycine ethyl ester.—Practically colorless rhombohedra from 25% alcohol. Sodium salt—lustrous cream-colored leaflets.

4-Ethoxyphenylglycine.—Cannot be obtained crystalline. Its monosodium salt, prepared like the corresponding methoxy compound, exists as yellow needles sparingly soluble in water.

4-Aminophenoxyacetic ethyl ester.—Lustrous, salmon-colored leaflets, m. p. 132-3° with decomposition, readily soluble in warm methyl or ethyl alcohol. Sodium salt—aggregates of brownish needles from 85% alcohol.

4-Aminophenoxyacetic acid.—Microscopic crystals melting and intumescing at 132°. Disodium salt—brown needles gradually darkening and decomposing on standing.

4-Aminophenoxyacetamide.—Cream-colored needles m. p. 162° with effervescence. Sodium salt—drab-colored needles soluble in water.

4-Aminophenoxyacet-methylamide.—Glistening cream-colored needles, m. p. 170° with decomposition. Sodium salt—pale yellow aggregates of hair-like needles.

4-Methylaminophenoxyacetic acid.—Greenish-yellow aggregates of microscopic spindles decomposing at 155-60°.

3-Methyl-4-aminophenoxyacetic methyl ester.—Minute needles, m. p. 105-7° with decomposition. Sodium salt—reddish-brown needles.

3-Methyl-4-aminophenoxyacetic acid.—Too unstable for isolation. Disodium salt—light-brown glistening plates.

2-Methyl-4-aminophenoxyacetic methyl ester.—Purple-brown leaflets, decomposing at 143-4°, and soluble in hot methyl or ethyl alcohol.

2-Methyl-4-aminophenoxyacetic acid.—Too unstable to be isolated. Disodium salt—pinkish-yellow needles gradually decomposing on exposure.

2,5-Dimethyl-4-aminophenoxyacetic methyl ester.—Grayish-yellow needles decomposing at 120° and soluble in hot methyl alcohol. The disodium salt cannot be obtained pure.

2-Methyl-5-isopropyl-4-aminophenoxyacetic methyl ester.—Needles decomposing at 145°, and soluble in hot alcohol.

2-Methyl-5-isopropyl-4-aminophenoxyacetic acid.—Cannot be obtained. Its disodium salt is obtained as brown needles.

3-Methyl-6-isopropyl-4-aminophenoxyacetic methyl ester.—Yellow leaflets from 85% alcohol. When rapidly heated it intumesces at 130°, but on slowly raising the temperature it turns orange above 120°, and then gradually darkens but does not melt below 275°.

3-Methyl-6-isopropyl-4-aminophenoxyacetic acid.—Cannot be isolated. The disodium salt crystallizes in lustrous yellow leaflets.

2-Bromo-4-aminophenoxyacetic methyl ester.—Cream-colored needles decomposing at 154-5°.

2-Bromo-4-aminophenoxyacetic acid.—Pale yellow needles decomposing at 120° when anhydrous. Disodium salt—lustrous brownish-yellow needles.

6-Bromo-4-amino-2-methylphenoxyacetic methyl ester.—Pinkish needles intumescing at 188°. It forms a yellow sodium salt.

6-Bromo-4-amino-2-methylphenoxyacetic acid.—Grayish aggregates decomposing at 155°. The disodium salt is an indefinitely crystalline product easily soluble in water.

4-Amino-6-acetophenoxyacetic methyl ester.—Microscopic hair-like needles.

4-Amino-6-acetophenoxyacetic acid.—Has not been obtained pure. The disodium salt crystallizes in pale brown leaflets.

p-Azobenzenediarsonic acid, $H_2O_3AsC_6H_4.N = N.C_6H_4AsO_3H_2$, results upon condensing 4-nitroso- with 4-aminophenylarsonic acid in boiling glacial acetic acid,[999] or by allowing the corresponding hydrazo compound to oxidize in the air.[244] The product is a dark brown powder readily soluble in alkalis, less so in glacial acetic acid or hot water, sparingly in dilute mineral acids or cold water, and practically insoluble in the usual organic solvents. It yields a purple-red solution with concentrated mineral acids.

Azobenzene-4-arsonic acid, $C_6H_5.N = N.C_6H_4.AsO_3H_2$, prepared by condensing 4-nitrosophenylarsonic acid with aniline, is a brown amorphous powder readily soluble in ammonia, alkali hydroxides or carbonates, and sparingly so in water or dilute acids.[999]

Azo Dyes Derived from p-Arsanilic Acid.

Hydrochloride of -2-aminonaphthalene-1-azobenzene-4′-arsonic acid, $(HCl.H_2N)C_{10}H_6.N = N.C_6H_4AsO_3H_2$.—On diazotizing p-arsanilic acid and coupling with β-naphthylamine hydrochloride, the above compound separates as a red crystalline precipitate soluble in aqueous sodium carbonate.[1000] The product can be obtained free of hydrochloric acid by coupling in the presence of sodium acetate.

3-Methyl-4,6-diaminoazobenzene-4′-arsonic acid,

$$H_2O_3AsC_6H_4.N = N.C_6H_2(CH_3)(NH_2)_2,$$

is a dark red dye, soluble in caustic soda, made by coupling 4-diazophenylarsonic acid with m-tolylenediamine,[1001] or by condensing 4-nitrosophenylarsonic acid with hydroxylamine, and coupling the resulting antidiazotate with m-tolylenediamine.[1002]

4-[Phenyl-(4′-arsonic acid)azo]-phenylglycine.—Orange-red aggregates of minute, lenticular platelets with a golden luster, sintering, melting and slowly decomposing at 170-5°, and dissolving in dilute alkali, concentrated sulfuric or 1:1 hydrochloric acid. It is prepared by coupling 4-diazophenylarsonic acid with phenylglycine. The hydrochloride crystallizes in red needles with a purplish luster.[1003]

2-Methyl-4-[phenyl-(4′-arsonic acid)azo]-phenylglycine consists of red-brown needles, leaflets and rhombic platelets intumescing at 157°, and soluble in methyl alcohol or concentrated sulfuric acid. Its hydrochloride forms dark brown platelets.[1003]

2-Methoxy-4-[phenyl-(4′-arsonic acid)azo]-phenylglycine is obtained as lustrous, steel-blue aggregates of platelets intumescing at 167° when anhydrous; soluble in dilute aqueous alkali hydroxides or carbonates, concentrated sulfuric or 1:1 hydrochloric acid, and methyl or

hot ethyl alcohol. The monosodium salt crystallizes in nacreous, orange-red platelets containing $2\frac{1}{2}H_2O$, and is soluble in water.[1003]

2-Ethoxy-4-[phenyl-(4'-arsonic acid)azo]-phenylglycine.—Purplish-brown needles decomposing at 245-50°, soluble in alcohol, acetic or concentrated sulfuric acid. Its monosodium salt separates from 50% alcohol in orange-brown lustrous platelets soluble in water.[1003]

α'-[Phenyl-(4,-arsonic acid)azo]-α-naphthylglycine is a crystalline product melting wih decomposition at 275°, soluble in concentrated sulfuric acid. The disodium salt is readily soluble in water.[1004]

4-[Phenyl-(4'-arsonic acid)azo]-phenylaminomethylsulfonic acid, $H_2O_3AsC_6H_4.N=N.C_6H_4.NHCH_2SO_3H$, is produced by coupling 4-diazophenylarsonic acid with methylene-aniline sodium bisulfite, crystallizing in red needles readily soluble in concentrated sulfuric acid or hot water, and sparingly in cold water. When heated the anhydrous product sinters and partially melts at 187-9°. The disodium salt consists of orange-colored needles readily soluble in water.[1004]

2-Methoxy-4-phenyl-(4'-arsonic acid)azo-phenylaminomethylsulfonic acid.—Violet needles soluble in concentrated sulfuric acid, and melting when anhydrous at 158-60° with evolution of gas. Its soluble disodium salt forms orange-red needles.[1004]

4-Dimethylaminoazobenzene-4'-arsonic acid,

$$(CH_3)_2N.C_6H_4.N=N.C_6H_4AsO_3H_2.$$

When the crude product, obtained by coupling 4-diazophenylarsonic acid with dimethylaniline in hydrochloric acid solution, is purified through its monosodium salt, there results a red powder readily soluble in alkalis or mineral acids but insoluble in water or the usual solvents. The above salt separates from hot water in lustrous scarlet plates containing $5\frac{1}{2}$ molecules of water, while the disodium salt containing $6H_2O$ is a scarlet powder soluble in cold water.[957]

4-Hydroxyazobenzene-4'-arsonic acid,

$$HO.C_6H_4.N=N.C_6H_4AsO_3H_2.$$

Prepared by coupling 4-diazophenylarsonic acid with phenol in alkaline solution, acidifying with hydrochloric acid and purifying the crude product through the monosodium salt. It is a light red powder insoluble in water or the usual organic solvents, but readily dissolves in alkalis

2-Hydroxynaphthaleneazobenzene-4′-arsonic acid,

$$HO.C_{10}H_6.N=N.C_6H_4AsO_3H_2,$$

is a bright red, alkali-soluble powder which results on diazotizing p-arsanilic acid and coupling with alkaline β-naphthol solution. The monosodium salt, containing $5H_2O$, is a deep orange, crystalline precipitate sparingly soluble in boiling water. The disodium salt is a dark red powder readily soluble in water, and contains $6\frac{1}{2}H_2O$.[1006, 1007]

1-Amino-2-methoxynaphthalene-4-azobenzene-4′-arsonic acid.—Bluish-black, glistening platelets remaining unmelted below 285°, and dissolving in dilute caustic soda or concentrated sulfuric acid.[1008]

1-Amino-4-methoxynaphthalene-2-azobenzene-4′-arsonic acid consists of dark brown aggregates with a bronzy luster. It softens to a tar at about 195°, intumesces at about 225°, and is soluble in acetic acid, alcohol, dilute caustic soda or concentrated sulfuric acid.[1008]

3-Amino-6-[phenyl-(4′-arsonic acid)azo]-phenoxyacetic acid,

$$H_2O_3AsC_6H_4.N=N.C_6H_3(NH_2)(O.CH_2COOH).$$

Made in the usual manner by coupling with 3-aminophenoxyacetic acid, crystallizing in red, glistening needles soluble in 1:1 hydrochloric acid, concentrated sulfuric acid or dilute alkalis. The anhydrous product does not melt below 285°. Its hydrochloride consists of orange-brown microscopic crystals. The monosodium salt is an orange-colored microcrystalline compound.[1008]

4-Methyl-3-amino-6-[phenyl-(4′-arsonic acid)azo]-phenoxyacetic acid.—Dark red aggregates of needles intumescing at 242-3°, difficultly soluble in concentrated hydrochloric acid, but readily in dilute alkalis or concentrated sulfuric acid. It forms an orange-red hydrochloride and a red crystalline monosodium salt.[1009]

2-Methyl-5-amino-4-[phenyl-(4′-arsonic acid)azo]-phenoxyacetic acid consists of lustrous purplish-brown needles intumescing at 187-8°, readily soluble in methyl alcohol or concentrated sulfuric acid, less so in ethyl alcohol or concentrated hydrochloric acid. The hydrochloride separates as dull red microcrystals.[1009]

α-Amino-β-[phenyl-(4-arsonic acid)]azo-α′-naphthoxyacetic acid is obtained as dark red needles with a golden luster, decomposing at 285°, and dissolving in concentrated sulfuric acid. Its disodium salt forms dark brown felted needles readily soluble in water.[1010]

α-Amino-α′-[phenyl-(4-arsonic acid)]azo-β-naphthoxyacetic acid.—Red-brown microcrystalline aggregates remaining unmelted below 285°.

The disodium salt crystallizes in almost black aggregates of microscopic hairs soluble in water.[1010]

4-Amino-5-[phenyl-(4′-arsonic acid)azo]-1,2-phenylenedioxyacetic acid exists as purplish-brown microcrystals soluble in concentrated sulfuric acid, and when anhydrous does not melt below 280°. Its monosodium salt forms purplish-brown spherules sparingly soluble in water, but readily in dilute alkali hydroxides or carbonates.[1010]

2-Hydroxy-5-[phenyl-(4′-arsonic acid)azo]-phenoxyacetic acid.—Brown platelets remaining unmelted below 280°, soluble in dilute sodium hydroxide, concentrated sulfuric acid or boiling alcohol. Monosodium salt—yellow, indefinitely crystalline globules.[1011]

3-Amino-6-methoxy-4-[phenyl-(4′-arsonic acid)azo]-phenoxyacetic acid is obtained as glistening bronze needles soluble in methyl or ethyl alcohol, concentrated sulfuric or 1:1 hydrochloric acid, and dilute alkali hydroxides or carbonates. It sinters at 175-85°, but when anhydrous intumesces at 208-13°. Its hydrochloride exists as dark brown microscopic platelets.[1009]

4-Amino-6-methoxy-3-[phenyl-(4′-arsonic acid)azo]-phenoxyacetic acid.—Glistening maroon-colored platelets which do not melt below 280°, and dissolve in concentrated sulfuric or hot 1:1 hydrochloric acid. The monosodium salt crystallizes in chocolate-colored needles sparingly soluble in water but readily in dilute alkalis. The hydrochloride consists of dark red needles.[1010]

2-Amino-8-hydroxy-6-sulfonaphthaleneazobenzene-4′-arsonic acid, obtained from 4-diazophenylarsonic acid and 2-amino-8-hydroxynaphthalene-6-sulfonic acid (Gamma acid) in alkaline solution, is a dark violet-red powder easily soluble in water or methyl alcohol, but insoluble in chloroform or ether.[582]

2-Hydroxy-3,6-disulfonaphthaleneazobenzene-4′-arsonic acid is a red, water-soluble powder isolated in the usual manner by coupling with disodium-β-naphthol-3,6-disulfonate (R salt) in alkaline solution.[1007]

1-Amino-8-hydroxy-3,6-disulfonaphthalene-2-azobenzene-4′-arsonic acid, $(NH_2)(OH)(SO_3H)_2C_{10}H_3.N{=}N.C_6H_4AsO_3H_2$, made by coupling with 1,8-aminonaphthol-3,6-disulfonic acid (H acid) in either alkaline or acid solution, is a brownish-black powder easily soluble in water.[1007]

1-Carboxynaphthaleneazobenzene-4′-arsonic acid is a brownish-black powder soluble in water, obtained by coupling 4-diazophenylarsonic acid

4-Methylamino-5-carboxyphenylazobenzene-4′-arsonic acid.—Brick-red, glistening needles and plates not melting below 280°; soluble in concentrated sulfuric acid or dilute hydrochloric acid. On treating the latter solution with sodium nitrite, a pale salmon-colored precipitate is formed. The hydrochloride crystallizes in rosets of purplish-red plates; the monosodium salt in brownish-yellow microscopic needles, and the disodium salt in red needles readily soluble in water.[1005]

The corresponding *ethyl compound* is isolated as lustrous, deep orange colored platelets which do not melt below 275°, and are more soluble in methyl or boiling amyl alcohol than in the other neutral solvents.[1005]

The corresponding *isoamyl compound* forms orange-red glistening platelets soluble in concentrated sulfuric or hydrochloric acid or boiling alcohol. The hydrochloride separates in dark colored microscopic needles. The monosodium salt crystallizes in orange-colored leaflets very difficultly soluble in boiling water.[1012]

4-Amino-2,3-dimethoxy-5-carboxyphenylazobenzene-4′-arsonic acid.—Orange-red platelets easily soluble in methyl alcohol, concentrated sulfuric acid or boiling dilute hydrochloric acid, and does not melt below 275°. The hydrochloride forms brown platelets and needles, while the monosodium salt exists as brownish-orange needles.[1012]

2-Amino-4,5-dimethoxy-3-carboxyphenylazobenzene-4′-arsonic acid is obtained in brown leaflets and microcrystalline aggregates with a purplish luster. It decomposes somewhat upon heating, but remains unmelted up to 290°; is easily soluble in dilute alkalis or concentrated sulfuric acid, difficultly in the usual organic solvents, and only sparingly in concentrated hydrochloric acid. The hydrochloride separates as dark orange-red spherules. The monosodium salt consists of orange-red microcrystals turning chocolate-brown when air-dried. It is difficultly soluble in boiling water but readily in dilute alkalis.[1012]

Disazo Compounds Derived from p-Arsanilic Acid.

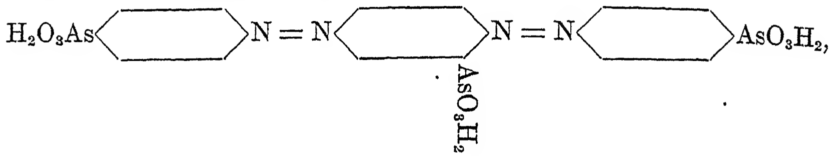
A disazo compound may be obtained from 1-amino-8-hydroxy-3,6-disulfonaphthalene-2-azobenzene-4′-arsonic acid by treating with 4-diazophenylarsonic acid in alkaline solution. The product is isolated as blue needles with a bronzy luster, soluble in water, acetic or concentrated sulfuric acid, and sparingly so in hot alcohol.[1013]

A similar product, consisting of a light brown powder, results upon diazotizing tolidine with two molecular proportions of sodium nitrite, and coupling with an alkaline solution of two moles of p-arsanilic acid.[582]

Disazobenzene-4,4'-diarsonic acid,

is a black powder with a metallic luster; soluble in alkalis or concentrated acids. It is obtained by condensing 4-nitrosophenylarsonic acid (2 mols.) with p-phenylenediamine in glacial acetic acid medium.[931]

Disazobenzene-4,2',4''-triarsonic acid,



similarly prepared from 2,5-diaminophenylarsonic acid and 4-nitrosophenylarsonic acid, is a black powder with a dark greenish luster, soluble in alkalis or concentrated acids.[932]

Trisazo and Tetraazo Compounds.

H acid—p-arsanilic acid
↗
Benzidine .—When benzidene is diazotized
↘
H acid

with sodium nitrite (2 moles) and coupled with H acid (2 moles) there is obtained a violet colored dye, which is converted into a trisazo dye upon treatment with an alkaline solution of 4-diazophenylarsonic acid (1 mole). The dried product is a brownish-black powder soluble in water to a blue solution.[1014]

S acid—p-arsanilic acid
↗
Dichlorobenzidine .—A bluish-black pow-
↘
H acid

der, soluble in water or aqueous sodium carbonate, results upon diazotizing dichlorobenzidine with sodium nitrite (2 moles), coupling with 1-amino-8-hydroxy-4-sulfonaphthaleneazobenzene-4'-arsonic acid, and combining the resulting product with H acid (1 mole) in alkaline solution.[1015]

H acid—p-arsanilic acid
↗
Benzidine .—The product thus obtained is

By substituting 2-amino-5-naphthol-4-sulfonic acid (2 moles) for the H acid in the preceding diagram, a water-soluble dye with a lustrous bronzy color is obtained, while with two moles of chromotropic acid there is formed a brownish-black powder soluble in water or aqueous sodium carbonate.[1015]

$$\textit{Tolidine}\begin{array}{l}\nearrow \textit{2-amino-5-naphthol-7-sulfonic acid—p-arsanilic acid}\\ \searrow \textit{2-amino-5-naphthol-7-sulfonic acid—p-arsanilic acid}\end{array}\text{.—A}$$

lustrous bronzy powder dissolving in water to a violet solution.[1014]

$$\textit{Chlorobenzidine}\begin{array}{l}\nearrow \textit{H acid—p-arsanilic acid}\\ \searrow \textit{H acid—p-arsanilic acid}\end{array}\text{.—The product is a dark}$$

brown powder yielding a deep blue aqueous solution.[1014] If S acid (2 moles) is substituted for H acid, the resulting dye is a brown powder soluble in water with a violet-blue color which turns blue upon the addition of aqueous sodium carbonate.[1015]

Triazo Compound.

4-Triazophenylarsonic acid, $H_2O_3AsC_6H_4.N_3$, is obtained as white crystals upon adding a solution of sodium azide to 4-diazophenylarsonic acid and recrystallizing from either dilute alcohol or dilute sulfuric acid. Its monosodium salt, prepared by boiling an alcoholic solution of the acid with sodium ethoxide, is a white powder readily soluble in water.[1016]

Azomethine Derivatives.

Benzylidene-p-arsanilic acid, $H_2O_3AsC_6H_4.N = HC.C_6H_5$, is formed as a by-product in the preparation of 1-(4′-arsonophenyl)-2-phenyl-4,5-diketopyrrolidine from p-arsanilic acid, benzaldehyde and pyruvic acid or ethyl pyruvate. It crystallizes from alcohol in heavy, white granular crystals melting with decomposition at 225°.[151]

4-Dimethylaminobenzylidine-p-arsanilic acid,

$$H_2O_3AsC_6H_4.N = CH.C_6H_4.N(CH_3)_2,$$

is prepared by heating together p-arsanilic acid and 4-dimethylaminobenzaldehyde. Both the free acid and its salts are colored orange-red.[1017]

4-Hydroxybenzylidine-p-arsanilic acid,

$$H_2O_3AsC_6H_4.N = CH.C_6H_4.OH,$$

results on heating molecular proportions of p-arsanilic acid and 4-hydroxybenzaldehyde at 140-50°. It is a yellow crystalline powder sparingly soluble in water or alcohol and insoluble in ether; is hydrolyzed by hot water, but upon cooling the components reunite. With mineral acids it forms salts such as $HCl(C_6H_5.CH = HN.C_6H_4AsO_3H_2)$. They may also be prepared directly by condensing p-arsanilic acid with 4-hydroxybenzaldehyde in concentrated water-alcohol solution in the presence of the particular mineral acid. The salts are yellow, hydrolyzable compounds readily dissolving in aqueous sodium carbonate, and more soluble in water than the free acid.[1017]

2,4-Dihydroxybenzylidene-p-arsanilic acid,

$$H_2O_3AsC_6H_4.N = CH.C_6H_3(OH)_2,$$

is a yellow crystalline powder obtained by condensing resorcylaldehyde with p-arsanilic acid.[1017]

10. *N-Substituted Derivatives of p-Arsanilic Acid.—4-Formylaminophenylarsonic acid,* $H_2O_3AsC_6H_4.NHCHO$, results on refluxing dry atoxyl with formic acid, distilling off the excess of the volatile acid and treating with water. It crystallizes from either hot water or methyl alcohol in colorless needles insoluble in ether, and is characterized by the ease with which the formyl group can be split off, cold dilute hydrochloric acid accomplishing this in a very short time.[1018]

4-Acetylaminophenylarsonic acid, $H_2O_3AsC_6H_4.NHCOCH_3$, may be prepared from crystalline atoxyl and acetic anhydride; by refluxing anhydrous atoxyl with glacial acetic acid and distilling off the excess of the latter; by condensing p-arsanilic acid with acetylchloride in pyridine, or with acetic anhydride in the presence of a little concentrated sulfuric acid;[988, 1018] or from 4-aminoacetanilide by Bart's method, using either sodium-[86] or potassium arsenite.[929] The compound forms white lustrous leaflets possessing but feebly basic properties. It is precipitated from solutions of its salts by an excess of mineral acids or from its concentrated hydrochloric acid solution upon dilution with water. It does not react with naphthoquinone sulfonic acid; is unaffected by heating above 200°, but is readily hydrolyzed by boiling with acids or alkalis. Its monosodium salt (*"Acetylatoxyl," "Arsacetin"*) crystallizes in white needles containing four or five molecules of water, and is obtained either by neutralizing the free acid,[1000] or directly by Bart's method.[86]

4-n-Butyrylaminophenylarsonic acid, $H_2O_3AsC_6H_4NHCOC_3H_7$, may

pyridine, precipitating with ether, and treating successively with water and hydrochloric acid; or by warming anhydrous atoxyl with n-butyric anhydride.[1018]

4-Benzoylaminophenylarsonic acid, $H_2O_3AsC_6H_4NHCOC_6H_5$.—From p-arsanilic acid and benzoyl chloride by the Schotten-Baumann reaction.[1018]

4-Carbethoxyaminophenylarsonic acid, $H_2O_3AsC_6H_4NHCOOC_2H_5$.—Needles, m. p. 330-40°; obtained by the action of ethylchlorocarbonate upon p-arsanilic acid in the presence of caustic soda.[1019, 322]

4-Phenylsulfoneaminophenylarsonic acid, $H_2O_3AsC_6H_4NHSO_2C_6H_5$, may be obtained from 4-phenylsulfoneaminophenylamine by Mouneyrat's modification of Bart's method,[89] or from p-arsanilic acid and benzenesulfonic chloride by the Schotten-Baumann reaction.[1020] In the latter method the yield is increased by employing sodium carbonate instead of the hydroxide.[1021] The sodium salt is known as *"Hectine"* and the mercury salt, as *"Hectargyre."*

4-Toluenesulfoneaminophenylarsonic acid, $H_2O_3AsC_6H_4NHSO_2C_7H_7$, produced from p-arsanilic acid and toluene-p-sulfonic chloride by the Schotten-Baumann reaction, crystallizes from hot water in colorless crystals. Its sodium salt is very soluble in water, slightly in alcohol.[1022]

4-Oxalylaminophenylarsonic acid (Oxanil-p-arsonic acid),

$$H_2O_3AsC_6H_4NHCOCOOH,$$

is prepared by heating either atoxyl or arsanilic acid with an excess of crystalline oxalic acid at 130-40° until all the water is removed, then further heating at 160° until pulverulent, and finally acidifying with dilute hydrochloric acid. It separates from 50% acetic acid as a white crystalline powder readily soluble in hot water, less so in glacial acetic acid, methyl or ethyl alcohol, and insoluble in acetone, ether, benzene or dilute mineral acids. It does not melt below 360°, and forms soluble salts with alkalis.[1023]

4-Malonylaminophenylarsonic acid, $H_2O_3AsC_6H_4NHCOCH_2COOH$, results when p-arsanilic acid is heated with ethyl malonate in a reflux apparatus. It is insoluble in ether.[1018]

4-Phthalylaminophenylarsonic acid, $H_2O_3AsC_6H_4NHCOC_6H_4COOH$, is obtained from p-arsanilic acid and phthalyl chloride in alkaline medium by the Schotten-Baumann reaction.[1018]

4-Chloroacetylaminophenylarsonic acid, $H_2O_3AsC_6H_4NHCOCH_2Cl$, is made either by dissolving p-arsanilic acid in warm chloroacetyl-

chloride, cooling and mixing with water;[1018] or by heating p-arsanilic acid with dry chloroacetic acid on the water-bath, and pouring the resulting mass into a saturated sodium chloride solution.[1024] It exists as minute platelets and leaflets which darken on rapid heating, but melt with decomposition when kept at 285° for a few moments. It is readily soluble in hot alcohol, sparingly in cold water, acetic acid or acetone, more soluble in hot water or acetic acid, and is slowly acted upon by moist air.

4-Iodoacetylaminophenylarsonic acid, $H_2O_3AsC_6H_4NHCOCH_2I$, separates upon treating p-arsanilic acid with iodoacetylchloride in alkaline solution at 0° and subsequently neutralizing. It exists as lustrous needles, m. p. 196° with decomposition, readily soluble in alkalis, but insoluble in acids or the usual organic solvents.[1025]

4-Iodopropionylaminophenylarsonic acid, $H_2O_3AsC_6H_4NHCOC_2H_4I$, similarly prepared from iodopropionylchloride, crystallizes in needles decomposing at 224°, readily soluble in alkalis, and insoluble in the usual organic solvents.[1025]

Symm. Diphenylurea-4,4′-diarsonic acid, $CO\begin{cases} HNC_6H_4AsO_3H_2 \\ HNC_6H_4AsO_3H_2 \end{cases}$, results on adding a calculated quantity of a 20% toluene solution of carbonyl chloride to aqueous atoxyl at low temperature.[1018]

4-Carbamidophenylarsonic acid, $H_2O_3AsC_6H_4NHCONH_2$.—Made by acidifying an aqueous solution of atoxyl and potassium cyanate with acetic acid, and saturating, after 24 hours, with hydrochloric acid.[962]

N-4-Methylcarbamidophenylarsonic acid,

$$H_2O_3AsC_6H_4NHCONHCH_3.$$

From methylisocyanate by reacting with aqueous atoxyl, and subsequently acidifying with hydrochloric acid.[962]

N-4-Phenylcarbamidophenylarsonic acid,

$$H_2O_3AsC_6H_4NHCONHC_6H_5.$$

Phenylisocyanate is added to a well-cooled, aqueous atoxyl solution, and the whole maintained at a low temperature for twelve hours. It is then extracted with ether, the aqueous layer separated, and the compound precipitated from the latter with hydrochloric acid.[962]

4-Thiocarbamidophenylarsonic acid, $H_2O_3AsC_6H_4NHCSNH_2$. — A saturated solution of p-arsanilic acid in aqueous potassium thiocyanate-

hydrochloric acid is evaporated to dryness, and the residue warmed for two hours. After cooling it is dissolved in dilute alkali and reprecipitated with dilute hydrochloric acid.[962]

N-4-Allylthiocarbamidophenylarsonic acid,

$H_2O_3AsC_6H_4NHCSNHC_3H_5$,

is obtained by treating p-arsanilic acid with allylthiocarbimide in methyl alcohol at 30-5°. It forms snow-white needles and leaflets, m. p. 185° with decomposition; practically insoluble in water or ethyl alcohol, and sparingly soluble in methyl alcohol.[963]

Glycyl-p-arsanilic acid, $H_2NCH_2CONHC_6H_4AsO_3H_2$.—Chloroacetylarsanilic acid is warmed with concentrated aqueous ammonia at 30° until solution is complete, allowed to stand over night, and the excess of ammonia boiled off, when the crude product crystallizes along with the corresponding amino compound. Separation is effected by means of dilute hydrochloric acid in which the latter is insoluble. The crude glycyl-p-arsanilic acid is first reprecipitated by sodium acetate, and then purified by dissolving in dilute caustic soda solution and reprecipitating with carbon dioxide. It forms minute, toothed, glistening, anhydrous plates which do not melt below 295°, and are very difficultly soluble in boiling water or 50% alcohol. It functions as a very weak acid, dissolving only in an excess of weak bases, such as ammonia, and is displaced from its salts by carbon dioxide.[1026]

Iminobisacetyl-p-arsanilic acid, $(H_2O_3AsC_6H_4NHCOCH_2)_2NH$, obtained as a by-product in the preparation of the preceding compound, consists of glistening rosets of microcrystals darkening at 280-5° without melting, and practically insoluble in the usual solvents.[1027]

N-Methylglycyl-p-arsanilic acid, $CH_3NHCH_2CONHC_6H_4AsO_3H_2$, is prepared by adding chloroacetylarsanilic acid to a methylamine solution, allowing to stand for 24 hours, removing the excess of methylamine on the water-bath, and finally acidifying with acetic acid. Recrystallized from water it separates as long, silky, glistening needles containing about $2H_2O$, turning brown but not melting below 275°, practically insoluble in hot alcohol, slightly soluble in boiling water, but readily in dilute mineral acids. On adding sodium nitrite to its dilute hydrochloric acid solution the nitroso derivative deposits on rubbing as sheaves and spheres of microscopic needles.[1027]

N-Phenylglycyl-p-arsanilic acid (N-Phenylglycineanilide-p'-arsonic acid), $C_6H_5NHCH_2CONHC_6H_4AsO_3H_2$.—This substance, isomeric with phenylglycineanilide-p-arsonic acid, is prepared by boiling together alcoholic aniline and alkaline chloroacetylarsanilic acid solutions for one-half hour under an air condenser. It crystallizes from 50% alcohol as

delicate, felted needles almost insoluble in boiling water and darkening slightly but not melting below 280°. On treating its suspension in hot 50 per cent acetic acid with an excess of sodium nitrite the nitroso derivative is formed.[1027]

p-Aminophenylglycyl-p-arsanilic acid,

$$H_2NC_6H_4NHCH_2CONHC_6H_4AsO_3H_2,$$

results upon hydrolyzing the succeeding acetylamino-compound with boiling hydrochloric acid, forming, when pure, microcrystalline aggregates which tend to become colloidal on washing with water. It is soluble in dilute mineral acids or alkalis, very sparingly so in boiling 50% alcohol, practically insoluble in boiling water, and may be readily diazotized, giving a red color with R-salt. When rapidly heated the acid darkens and sinters, but does not melt below 280°.[1028]

p-Acetylaminophenylglycyl-p-arsanilic acid,

$$H_2O_3AsC_6H_4NHCOCH_2NHC_6H_4NHCOCH_3,$$

is prepared like the previous compounds using p-aminoacetanilide. It forms glistening, hexagonal platelets which do not melt below 275° and are very sparingly soluble in boiling water or 50% alcohol. Its sodium salt crystallizes in flat glistening needles containing seven molecules of water of crystallization.[1028]

m-Oxalylaminophenylglycyl-p-arsanilic acid,

$$HOOCCONHC_6H_4NHCH_2CONHC_6H_4AsO_3H_2,$$

made by boiling a solution of chloroacetylarsanilic acid and m-amino-oxanilic acid in aqueous caustic soda, is isolated as the hydrochloride, composed of aggregates of microscopic plumes which gradually lose hydrochloric acid on standing in moist air.

The free acid may be obtained by boiling the hydrochloride with water. It crystallizes with $1H_2O$, is practically insoluble in boiling water, and very sparingly soluble in 50% alcohol. When rapidly heated to 175°, then slowly, the anyhydrous acid effervesces at 179°, with preliminary softening and darkening.[1029]

p-Oxalylaminophenylglycyl-p-arsanilic acid is prepared like its meta isomer, and forms slightly purplish aggregates of microscopic crystals containing 1.5 molecules of water of crystallization. It is almost insoluble in boiling water, very sparingly soluble in boiling 50% alcohol, and, when anhydrous, darkens above 200°, but does not melt below 275°. On heating with aqueous alkali the principal products recovered are either the unchanged oxamino compound or arsanilic acid, depending on the length of heating and the strength of the alkali. Heating, however, with 1:1 hydrochloric acid yields the amino compound.[1028]

p-Uraminophenylglycyl-p-arsanilic acid,

$$H_2NCONHC_6H_4NHCH_2CONHC_6H_4AsO_3H_2,$$

is made from chloroacetylarsanilic acid and p-aminophenylurea, crystallizing in spherular masses of microscopic leaflets soluble in boiling 50% alcohol, but very sparingly in water. When rapidly heated it changes color above 150° and darkens markedly at about 210°, but does not melt below 285°.[1030]

p-Oxamylaminophenylglycyl-p-arsanilic acid,

$$H_2NCOCONHC_6H_4NHCH_2CONHC_6H_4AsO_3H_2.$$

From chloroacetyl arsanilic acid and p-aminooxanilamide. Clusters of microscopic needles remaining unmelted below 285°, and practically insoluble in boiling water or 50% alcohol.[1030]

N-Phenylglycineanilide-p-glycineamide-p′-arsonic acid,

$$H_2O_3AsC_6H_4NHCOCH_2NHC_6H_4NHCH_2CONH_2,$$

is obtained from carefully purified p-aminophenylglycineamide as crusts of spherical aggregates of microcrystals which become ochreous in color on exposure to the air. When air-dried it contains about 1.5 molecules of water of crystallization. The anhydrous substance darkens at about 200°, but does not melt below 285°, and is rather sparingly soluble in boiling water or 50% alcohol.[1031]

m-Hydroxyphenylglycyl-p-arsanilic acid,

$$HOC_6H_4NHCH_2CONHC_6H_4AsO_3H_2,$$

obtained from m-aminophenol, is purified through its hydrochloride separating as pale pink, wedge-shaped, microscopic prisms containing 3.5 molecules of water of crystallization. On rapid heating it melts at about 80° in its water of crystallization, then quickly resolidifies, and on further heating turns purple at about 180°, gradually softening and charring as the temperature is raised. The compound is easily soluble in methyl or ethyl alcohol, acetone or boiling water, separating from the latter on cooling as a caseous mass. It is less readily soluble in glacial acetic acid, from which it separates in a different form, presumably due to dehydration. The hydrochloride consists of slightly purplish microcrystals which do not melt up to 280° and lose most of the halogen on boiling with water.[1032]

p-Hydroxyphenylglycyl-p-arsanilic acid is prepared from p-aminophenol and forms aggregates of microscopic hairs containing approximately one molecule of water of crystallization. The substance is almost insoluble in boiling water or 50% alcohol, and, when anhydrous, blackens and sinters above 200°, but does not melt entirely below 280°.

Its sodium salt consists of microscopic needles containing $1H_2O$, and is sparingly soluble in water at 0°, but readily on warming, the solution slowly developing a pale lilac color with ferric chloride.[1032]

N-Phenylglycineanilide-p-hydroxyacetic ether acid-p'-arsonic acid, $H_2O_3AsC_6H_4NHCOCH_2HNC_6H_4OCH_2COOH$, prepared from chloroacetylarsanilic acid and p-aminophenoxyacetic acid, crystallizes as minute, pale brown, wedge-shaped plates containing 1.5 molecules of water of crystallization. The substance is almost insoluble in boiling water or 50% alcohol, darkens, when anhydrous above 180°, and decomposes at about 275°.[1033]

N-Phenylglycineanilide-p-hydroxyacetic ether acid amide-p'-arsonic acid, $H_2O_3AsC_6H_4NHCOCH_2NHC_6H_4OCH_2CONH_2$, is made from p-aminophenoxyacetamide, separating as woolly masses of delicate needles practically insoluble in boiling water or 50% alcohol, and darkening somewhat but not melting below 265°.[1034]

The sodium salt crystallizes with four molecules of water in the form of slightly grayish rosets of flat, glistening needles. Its dilute aqueous solution gives immediate precipitates with silver or copper ions, a slow-forming, crystalline precipitate with calcium ions, and none with barium ions.

N-Phenylglycineanilide-p-hydroxyacetic ether acid ureide-p'-arsonic acid, $H_2O_3AsC_6H_4NHCOCH_2NHC_6H_4OCH_2CONHCONH_2$. — Feathery aggregates of minute platelets from p-aminophenoxyacetylurea. The substance is almost insoluble in boiling water or 50% alcohol, and when rapidly heated to 255°, then slowly, decomposes at 257-8° with preliminary darkening. The sodium salt crystallizes with 4 molecules of water as minute leaflets.[1034]

m-Carboxamidophenylglycyl-p-arsanilic acid,

$$H_2NCOC_6H_4NHCH_2CONHC_6H_4AsO_3H_2,$$

is made from m-aminobenzamide and purified through its sodium salt, which separates as radiating masses of flat needles containing one molecule of water of crystallization. The free acid crystallizes in microscopic needles very difficultly soluble in boiling water or acetic acid, but dissolving somewhat more easily in boiling 50% alcohol. When rapidly heated to 245°, then slowly, it darkens and decomposes at 248°.[1035]

p-Carboxamidophenylglycyl-p-arsanilic acid. — Derived from p-aminobenzamide as microscopic prisms which do not melt below 275° and are practically insoluble in boiling water or 50% alcohol. The sodium salt, glistening platelets containing $2H_2O$, is quite sparingly soluble in ice water, but more easily on warming.[1036]

N-Phenylglycineanilide-m-carboxureide-p′-arsonic acid,

$H_2O_3AsC_6H_4NHCOCH_2NHC_6H_4CONHCONH_2$.

From m-aminobenzoylurea as spherules of microscopic needles decomposing with darkening at about 280°, and almost insoluble in boiling water or 50% alcohol. The sodium salt crystallizes with three molecules of water as flat, microscopic needles.[1036]

N-Phenylglycineanilide-p-acetamide-p′-arsonic acid,

$H_2O_3AsC_6H_4NHCOCH_2NHC_6H_4CH_2CONH_2$.

Aggregates of microscopic platelets from p-aminophenylacetamide; is sparingly soluble in boiling water, more easily in boiling 50% alcohol or acetic acid. It darkens and softens above 180°, decomposing finally at 256-8°.[1033]

N-Phenylglycineanilide-p-acetureide-p′-arsonic acid,

$H_2O_3AsC_6H_4NHCOCH_2NHC_6H_4CH_2CONHCONH_2$,

is obtained from p-aminophenylacetylurea as rosets of microscopic hairs containing 0.5 molecule of water of crystallization, and sparingly soluble in boiling water or 50% alcohol. The anhydrous compound darkens above 230° and decomposes at 270-3°.[1033]

p-Acetophenylglycyl-p-arsanilic acid,

$CH_3COC_6H_4NHCH_2CONHC_6H_4AsO_3H_2$,

is prepared from p-aminoacetophenone, the pure compound existing as radiating masses of faintly yellow, microscopic needles which darken and decompose partially when heated, but do not melt below 290°. It is practically insoluble in boiling water and only very sparingly so in boiling 50% alcohol. The sodium salt crystallizes with 3 molecules of water as minute, narrow, pale yellow, glistening platelets sparingly soluble in cold water.[1037]

N-Phenylglycineanilide-4,4′-diarsonic acid,

$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4AsO_3H_2$,

from p-arsanilic acid and chloroacetyl-p-arsanilic acid, forms sheaves of microscopic needles containing 0.5 molecule of water of crystallization. The anhydrous substance does not melt up to 280°, is insoluble in boiling water and but very sparingly soluble in hot 50% alcohol.[1031]

Phenoxyacetyl-p-arsanilic acid, $C_6H_5OCH_2CONHC_6H_4AsO_3H_2$, is prepared from arsanilic acid and phenoxyacetyl chloride in sodium acetate solution; or by boiling a solution of chloroacetyl-p-arsanilic acid in N-aqueous caustic soda with phenol under an air condenser. Color-

less microscopic crystals or wedge-shaped plates and prisms which do not decompose below 280°, are soluble in boiling acetic acid, methyl or hot 50% ethyl alcohol, and very sparingly so in boiling water.[1038]

4'-Oxalylamino-phenoxyacetyl-p-arsanilic acid,

$$H_2O_3AsC_6H_4NHCOCH_2OC_6H_4NHCOCOOH,$$

is made from chloroacetylarsanilic acid and p-hydroxyoxanilamide, each dissolved in theoretical amounts of N-sodium hydroxide solution. It crystallizes with one molecule of water as cream-colored microscopic crystals unmelted below 280°, and appreciably soluble in boiling water or 50% alcohol.[1039]

4'-Uramino-phenoxyacetyl-p-arsanilic acid,

$$H_2O_3AsC_6H_4NHCOCH_2OC_6H_4NHCONH_2,$$

produced from chloroacetylarsanilic acid and p-hydroxyphenylurea in alkaline medium, is isolated through the sodium salt as aggregates of microscopic spindles practically insoluble in boiling water or 50% alcohol, and decomposing at about 280-3° with preliminary darkening. Its sodium salt crystallizes with 3 molecules of water as radiating masses of minute needles.[1039]

2'-Carboxamidophenoxyacetyl-p-arsanilic acid,

$$H_2O_3AsC_6H_4NHCOCH_2OC_6H_4CONH_2,$$

is obtained from salicylamide as delicate needles which do not decompose below 280°, are appreciably soluble in boiling 50% alcohol or acetic acid, less readily in the other hot solvents. Its sodium salt crystallizes with 5.5 molecules of water as prismatic needles.[1040]

4'-Carboxamidophenoxyacetyl-p-arsanilic acid, derived from p-hydroxybenzamide, is isolated through its sodium salt as long, glistening needles remaining unmelted below 280°, and practically insoluble in the usual solvents. The sodium salt crystallizes with 7.5 molecules of water as rosets of long, flat, delicate needles.[1040]

Phenyl-(4-arsonic acid)glycine [Phenylglycine-4-arsonic acid],

$$HOOCCH_2HNC_6H_4AsO_3H_2,$$

results on refluxing atoxyl with aqueous chloroacetic acid for 6-8 hours; or on heating p-arsanilic acid, sodium cyanide, 40% formaldehyde and water in an autoclave for one to two hours, neutralizing the cooled solution, and then hydrolyzing the resulting nitrile with caustic soda. The compound is sparingly soluble in cold water, but readily in concentrated hydrochloric acid, alkali hydroxides, carbonates or acetates, hot water or dilute hydrochloric acid.[1041]

N-(Phenyl-4-arsonic acid)-α-phenylglycine,

$$H_2O_3AsC_6H_4NHCH(C_6H_5)COOH,$$

may be prepared either from p-arsanilic acid and α-phenylchloroacetic acid, or by boiling the corresponding amide, described below, with 10% caustic soda solution. The compound crystallizes in lustrous, rhombic plates sparingly soluble in cold, more readily in warm water, alcohol or acetic acid, and fairly soluble in methyl alcohol. It effervesces at 202-3° with previous darkening and sintering.[1042]

4-Sulfomethylaminophenylarsonic acid, $H_2O_3AsC_6H_4NHCH_2SO_3H$, obtained by treating formaldehydesodiumbisulfite with a concentrated aqueous solution of atoxyl, and subsequently acidifying with dilute hydrochloric acid, forms snow-white needles decomposing at 148°. Its disodium salt is very soluble in water.[1043]

N-(Phenyl-4-arsonic acid)glycine methyl ester,

$$H_2O_3AsC_6H_4NHCH_2COOCH_3,$$

is prepared by refluxing for two hours a mixture of the preceding compound, dry methyl alcohol and a little concentrated sulfuric acid, and subsequently precipitating with water. It crystallizes from hot water or hot 95% alcohol in microscopic needles and thin plates, very sparingly soluble in cold water, cold alcohol or boiling acetone, and fairly easily in methyl alcohol, especially on warming. It decomposes at 285° with preliminary softening and darkening.[1044]

N-(Phenyl-4-arsonic acid)glycine ethyl ester,

$$H_2O_3AsC_6H_4NHCH_2COOC_2H_5,$$

prepared like the corresponding methyl ester, crystallizes from 50% alcohol in flat, delicate needles which melt and decompose at about 270° with preliminary darkening and softening. It is very difficultly soluble in cold water, but more soluble in cold alcohol, dissolving quite readily in either solvent on boiling.[1045]

N-(Phenyl-4-arsonic acid)glycineamide, [Phenylglycineamide-4-arsonic acid, "Tryparsamide"], $H_2O_3AsC_6H_4NHCH_2CONH_2$, results upon refluxing an aqueous atoxyl solution with chloracetamide,[1046] or from the action of ammonia upon N-(phenyl-4-arsonic acid)glycine methyl ester.[1045] It separates as long, thin, lustrous plates readily soluble in hot water, acetic acid, or cold concentrated hydrochloric acid, sparingly in cold water, dilute hydrochloric acid, hot methyl or ethyl alcohol, and insoluble in cold methyl alcohol, acetone or chloroform. On boiling its solution in sodium hydroxide, ammonia is evolved. When rapidly heated it darkens and softens at 280° without melting.

Salts.—The monosodium salt is extremely soluble in cold water, nd is prepared by neutralizing an aqueous suspension of the arsonic acid rith 25% sodium hydroxide and subsequently precipitated with alcohol. 'he potassium and ammonium salts are prepared in the same way, nd form thin, glistening, hexagonal, microscopic platelets. On addig a calcium chloride solution to a solution of the sodium salt, the alcium salt gradually separates as microscopic, wedge-shaped prisms ontaining no water of crystallization. Magnesia mixture causes no recipitate in the cold, but on warming the magnesium salt separates s a microcrystalline powder. Heavy metal salts give immediate preipitates, the silver salt forming aggregates of thin microscopic eedles.

N-(Phenyl-4-arsonic acid)-α-methylglycineamide, or *N-(Phenyl-4-rsonic acid)-α-aminopropionamide,* $H_2O_3AsC_6H_4NHCH\begin{matrix} CH_3 \\ CONH_2 \end{matrix}$.— 'rom p-arsanilic acid, dissolved in sodium hydroxide solution, by boilıg with α-bromopropionamide for about an hour. The product is ppreciably soluble in water at room temperature and readily on boiling, rystallizing on cooling as long, thin, hexagonal plates. It is also oluble in hot 50% alcohol. When rapidly heated it darkens above 255° nd decomposes at 262-3.5°. Its sodium salt crystallizes from 95% lcohol as long, flat, microscopic needles containing about $2\frac{1}{2}H_2O$ after ir-drying.[1047]

N-(Phenyl-4-arsonic acid)-α-phenylglycineamide,

$$H_2O_3AsC_6H_4NHCH(C_6H_5)CONH_2,$$

s made by boiling atoxyl, sodium iodide, phenylchloroacetamide and lcohol. The pure acid separates as microscopic needles which do not nelt below 280°, and are sparingly soluble in boiling water or 50% lcohol. Its sodium salt crystallizes with $3\frac{1}{2}$-$5H_2O$ as granular aggreates of plates readily soluble in water or boiling alcohol.[1048]

Oxanilamide-p-arsonic acid (p-Oxamylaminophenylarsonic acid), $I_2O_3AsC_6H_4NHCOCONH_2$.—Anhydrous atoxyl is heated with ethyl xamate for two hours at 140-50°, the mixture digested with water nd acidified with acetic acid. Minute needles which neither darken ıor melt below 280°, and are sparingly soluble in boiling water or 50% ılcohol. On boiling its dilute sodium hydroxide solution, ammonia is volved.[1047]

N-(Phenyl-4-arsonic acid) glycine methylamide,

$$H_2O_3AsC_6H_4NHCH_2CONHCH_3,$$

is made by refluxing an aqueous atoxyl solution with chloroacetylmethylamine. It separates as thin microscopic plates fairly easily soluble in hot water, from which it crystallizes in aggregates of curved spears. The substance is difficultly soluble in methyl alcohol, more readily in hot 50% ethyl alcohol, and decomposes at 285° with previous darkening and softening.[1049]

N-(Phenyl-4-arsonic acid) glycine ethylamide,

$$H_2O_3AsC_6H_4NHCH_2CONHC_2H_5,$$

is formed by condensing p-arsanilic acid and chloroacetylethylamine as in the previous compound. It is readily soluble in methyl alcohol, warm ethyl alcohol or water, but only sparingly so in the latter two at ordinary temperature. It darkens above 250° and decomposes at 278-80°.[1049]

N-(Phenyl-4-arsonic acid) glycine-n-propylamide,

$$H_2O_3AsC_6H_4NHCH_2CONHC_3H_7.$$

From p-arsanilic acid and chloroacetylpropylamine. It consists of flat needles, plates or wedge-shaped prisms, sparingly soluble in boiling water, but readily so in boiling 50% alcohol, from which it separates on cooling as sheaves of microscopic needles. It does not melt below 280°.[1049]

N-(Phenyl-4-arsonic acid) glycineanilide,

$$H_2O_3AsC_6H_4NHCH_2CONHC_6H_5,$$

may be prepared from atoxyl and chloro (or, better, iodo) acetanilide, or from N-(phenyl-4-arsonic acid) glycine methyl ester and aniline by the methods described in the preparation of the corresponding glycineamide. It crystallizes from 50% alcohol as minute delicate needles practically insoluble in the usual organic solvents at ordinary temperature, appreciably soluble in hot glacial acetic acid, methyl or ethyl alcohol, or dilute hydrochloric acid, the hydrochloride separating from the latter on cooling. The arsonic acid does not melt below 285°, and exhibits the characteristic property of a secondary amine in forming a nitroso compound with nitrous acid. The sodium salt consists of glistening scales containing four molecules of water of crystallization. It is freely soluble in water, the dilute solution yielding no immediate precipitate with calcium or barium salts. With magnesia mixture a precipitate is formed only on heating, while heavy metal salts give insoluble precipitates at once.[1050]

N-(Phenyl-4-arsonic acid)glycine-2′-toluidide,

$$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4CH_3,$$

is obtained in the usual manner from chloracetyl-o-toluidine, in the presence of a little sodium iodide. It crystallizes from 50% alcohol in woolly masses of delicate needles which do not melt below 275°; are readily soluble in hot acetic acid, sparingly in hot water or acetone, insoluble in cold, but appreciably soluble in boiling ethyl alcohol or cold methyl alcohol. Its sodium salt separates as aggregates of long, narrow platelets containing 2.5 molecules of water of crystallization.[1051]

N-(Phenyl-4-arsonic acid)glycine-3′-toluidide is derived from chloroacetyl-m-toluidine as aggregates of long, thin plates decomposing at about 285°, with preliminary darkening and softening. It is insoluble in boiling water or acetone, appreciably soluble in boiling methyl or ethyl alcohol, and readily in boiling acetic acid.[1052]

N-(Phenyl-4-arsonic acid)glycine-4′-toluidide, from chloroacetyl-p-toluidine, consists of minute needles which do not decompose below 280°; are practically insoluble in boiling water, sparingly soluble in boiling methyl or ethyl alcohol, but readily in boiling acetic acid. Its sodium salt separates as long, thin, curved, glistening needles containing $3H_2O$, and sparingly soluble in cold water, even less so in the presence of other sodium salts.[1052]

N-(Phenyl-4-arsonic acid)glycine benzylamide,

$$H_2O_3AsC_6H_4NHCH_2CONHCH_2C_6H_5,$$

resulting upon the prolonged refluxing of a mixture of atoxyl, chloroacetylbenzylamine, sodium iodide and alcohol, crystallizes from hot 85% alcohol as microscopic needles soluble in boiling 50% or 85% ethyl alcohol or boiling methyl alcohol, but very sparingly in boiling water. It decomposes at 282-4°.[1053]

N-(Phenyl-4-arsonic acid)glycine-α-naphthylamide,

$$H_2O_3AsC_6H_4NHCH_2CONHC_{10}H_7,$$

is made from chloroacetyl-α-naphthylamine, and consists of aggregates of microscopic needles practically insoluble in boiling water or 50% alcohol. When rapidly heated it darkens slightly, but does not melt up to 280°. On heating in dilute sodium hydroxide solution the odor of α-naphthylamine is quickly noticeable.[1052]

N-(Phenyl-4-arsonic acid)glycine-β-naphthylamide results when chloroacetyl-β-naphthylamine reacts with atoxyl in the presence of sodium iodide. Microscopic needles decomposing at 285-6° to a red

liquid, and practically insoluble in boiling water or 50% alcohol. Its sodium salt crystallizes from 50% alcohol as flat needles containing about 4.5 molecules of water of crystallization.[1054]

N-(Phenyl-4-arsonic acid) glycinediphenylamide,

$$H_2O_3AsC_6H_4NHCH_2CON(C_6H_5)_2,$$

is produced on boiling equivalent amounts of atoxyl, chloroacetyldiphenylamine and sodium iodide in 50% alcohol as in previous examples. It forms long, thin, microscopic leaflets containing one molecule of water of crystallization. The anhydrous substance decomposes at 271-2° with slight preliminary softening, and is very sparingly soluble in boiling water or 50% alcohol.[1054]

N-(Phenyl-4-arsonic acid) glycine-4'-chloroanilide,

$$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4Cl,$$

is obtained through its sodium salt as toothed, microscopic leaflets which are often cross shaped. It does not melt below 280°, and is almost insoluble in boiling water or 50% alcohol. The sodium salt is easily salted out from its solutions by sodium acetate.[1055]

N-(Phenyl-4-arsonic acid) glycine-4'-iodoanilide.—From chloroacetyl-p-iodoaniline. When purified through its sodium salt, it forms broad, minute needles which do not melt below 275°, and are practically insoluble in boiling water. Its sodium salt crystallizes from 85% alcohol in rosets of needles containing $3\frac{1}{2}H_2O$.[1055]

N-(Phenyl-4-arsonic acid) glycine-4'-nitroanilide,

$$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4NO_2.$$

For this compound chloroacetyl-p-nitroaniline is used, the substance crystallizing as long, thin, faintly yellow needles practically insoluble in boiling water or 50% alcohol, and remaining unmelted below 285°.[1055]

N-(Phenyl-4-arsonic acid) glycine-4'-aminoanilide,

$$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4NH_2,$$

may be prepared either by reducing the preceding nitro compound with freshly precipitated ferrous hydroxide, or by saponifying the following acetylamino derivative with hydrochloric acid. It separates as colorless, microscopic needles or platelets decomposing at 253-4° with preliminary darkening, practically insoluble in boiling water or 50% alcohol, and soluble in dilute hydrochloric acid, the hydrochloride being precipitated by an excess of the acid. The compound is readily diazotized, coupling with R-salt to form a red dye.[1056]

N-(Phenyl-4-arsonic acid) glycine-4′-acetylaminoanilide,

$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4NHCOCH_3$,

is made by heating atoxyl and p-chloroacetylaminoacetanilide for four hours. It is isolated through its sodium salt as aggregates of microscopic needles which are practically insoluble in boiling water or 50% alcohol, and do not melt below 285°. Its sodium salt consists of minute, lustrous, somewhat efflorescent platelets.[1057]

N-(Phenyl-4-arsonic acid) glycine-4′-acetylaminobenzylamide,

$H_2O_3AsC_6H_4NHCH_2CONHCH_2C_6H_4NHCOCH_3$,

results when p-arsanilic acid is boiled with p-acetylaminochloroacetylbenzylamine, and separates as flat, microscopic needles almost insoluble in the usual solvents except hot 50% alcohol, from which it separates on cooling as diamond-shaped plates. It darkens and sinters partly, but does not melt below 280°. The sodium salt, containing $4\frac{1}{2}H_2O$ exists as microscopic needles readily soluble in water.[1058]

N-(Phenyl-4-arsonic acid) glycine-3′-methyl-4′-acetylaminobenzylamide, $H_2O_3AsC_6H_4NHCH_2CONHCH_2C_6H_3(CH_3)NHCOCH_3$, is formed on condensing p-arsanilic acid with 3-methyl-4-acetylaminochloroacetylbenzylamine as an amorphous mass, which can be obtained crystalline by purification through its sodium salt. The free acid separates from 50% alcohol as flat, minute needles decomposing at 278°, and soluble in boiling water or 50% alcohol.[1059]

N-(Phenyl-4-arsonic acid) glycine-4′-uraminoanilide,

$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4NHCONH_2$,

derived from atoxyl and p-chloroacetylaminophenylurea, and subsequently isolating through the sodium salt, exists as pale brown, microcrystalline aggregates containing $\frac{1}{2}H_2O$. It is very sparingly soluble in boiling water, methyl or 50% ethyl alcohol, and decomposes, when anhydrous, at 230°, with preliminary darkening. Its sodium salt crystallizes in colorless microscopic needles containing $4H_2O$, and is soluble in hot water.[1057]

N-(Phenyl-4-arsonic acid) glycine-4′-methyl-5′-uraminoanilide,

$H_2O_3AsC_6H_4NHCH_2CONHC_6H_3(CH_3)NHCONH_2$.

Starting with 5-chloroacetylamino-2-methylphenylurea, the acid is finally isolated as microscopic platelets and hairs containing about one-half molecule of water of crystallization. The anhydrous substance decomposes at 257-8°, with preliminary darkening and sintering, and is practically insoluble in the usual solvents. Its sodium salt is readily soluble in water.[1060]

N-(Phenyl-4-arsonic acid)glycine-4′-uraminobenzylamide,

$$H_2O_3AsC_6H_4NHCH_2CONHCH_2C_6H_4NHCONH_2,$$

is prepared from p-arsanilic acid and p-uraminochloroacetylbenzylamine. Its sodium salt cannot be obtained crystalline by any of the usual methods.[1058]

N-(Phenyl-4-arsonic acid)-α-phenylglycine-4′-uraminoanilide,

$$H_2O_3AsC_6H_4NHCH(C_6H_5)CONHC_6H_4NHCONH_2,$$

is derived from arsanilic acid and p-phenylchloroacetylaminophenylurea as a gummy mass which gradually hardens. It decomposes at about 255° with preliminary darkening and softening, and is soluble in boiling 50% alcohol, but very difficultly in boiling water.[1061]

N-(Phenyl-4-arsonic acid)glycine-3′-oxamylaminoanilide,

$$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4NHCOCONH_2,$$

is obtained as slightly purplish, microcrystalline aggregates when m-chloroacetylaminooxanilamide is boiled for six hours with the usual reaction mixture. It is almost insoluble in boiling water, but very sparingly soluble in boiling 50% alcohol. When heated it gradually darkens and partly decomposes, but does not melt up to 280°.[1062]

N-(Phenyl-4-arsonic acid)glycine-4′-oxamylaminoanilide.—Owing to the insolubility of p-chloroacetylaminooxanilamide the heating is continued for a long time. The product forms microscopic needles insoluble in all neutral solvents, and does not melt below 280°.[1062]

N-(Phenyl-4-arsonic acid)glycyl-2′-aminophenol, or N-(Phenyl-4-arsonic acid)glycine-2′-hydroxyanilide,

$$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4OH.$$

From o-chloroacetylaminophenol without the aid of sodium iodide, the product consisting of lustrous crystals which melt and decompose at 190° with preliminary darkening. It is soluble in cold 95% alcohol, but more readily in boiling water, from which it separates on cooling as long, narrow, glistening leaflets. An alkaline solution couples readily with diazotized sulfanilic acid, yielding an orange colored solution.[1062]

N-(Phenyl-4-arsonic acid)glycyl-3′-aminophenol has also been prepared, but not yet described in the literature.[1063]

N-(Phenyl-4-arsonic acid)glycyl-4′-aminophenol, or N-(Phenyl-4-arsonic acid)glycine-4′-hydroxyanilide, is obtained from atoxyl and p-chloroacetylaminophenol as faintly pink, glistening platelets, darkening and melting to a black tar at 255-60°, and almost insoluble in

boiling water, 50% alcohol, 50% acetic acid or methyl alcohol. Its sodium salt is fairly soluble in cold water, and consists of lustrous platelets containing 4.5 molecules of water of crystallization.[1064]

N-(Phenyl-4-arsonic acid)-α-phenylglycine-3′-hydroxyanilide,

$$H_2O_3AsC_6H_4NHCH(C_6H_5)CONHC_6H_4OH,$$

is produced from m-phenylchloroacetylaminophenol, the pure product finally separating as purplish lenticular, microscopic platelets containing 1.5 molecules of water and effervescing at 155-60°. It is insoluble in hot acetone, appreciably soluble in methyl or ethyl alcohol, or boiling water, separating from the latter on cooling as an emulsion. When rapidly heated to 155°, then slowly, the anhydrous acid softens at about 155-60°, finally melting with the evolution of gas at about 200-10°.[1061]

N-(Phenyl-4-arsonic acid)glycine-2′-methyl-5′-hydroxyanilide,

$$H_2O_3AsC_6H_4NHCH_2CONHC_6H_3(CH_3)OH,$$

is made from atoxyl and 4-methyl-5-chloroacetylaminophenol, forming glistening, pink platelets and microscopic prisms very sparingly soluble in boiling water, acetic acid, methyl or ethyl alcohol, and decomposing at 220-5° with preliminary darkening. In alkaline solution it couples with diazotized sulfanilic acid yielding a redder color than do similar compounds in which the position para to the hydroxy group is unoccupied.[1064]

N-(Phenyl-4-arsonic acid)glycine-4′-methyl-5′-hydroxyanilide is similarly obtained from atoxyl and 2-methyl-5-chloroacetylaminophenol. When isolated through the sodium salt, it yields prisms and branched leaflets which are very sparingly soluble in the usual solvents, and decompose at 258° with preliminary darkening and softening. It may be readily coupled, in alkaline solution, with diazotized sulfanilic acid.[1064]

N-(Phenyl-4-arsonic acid)glycyl-1′-amino-2′-naphthol,

$$H_2O_3AsC_6H_4NHCH_2CONHC_{10}H_6OH.$$

From a mixture of atoxyl, sodium iodide, 1-chloroacetylamino-2-naphthol and alcohol by boiling for one hour. It separates as aggregates of microscopic plates and prisms containing $2H_2O$, almost insoluble in water, appreciably soluble in boiling alcohol or acetic acid, and readily in methyl alcohol. The anhydrous substance decomposes at 189-91° with preliminary darkening and softening.[1065]

N-(Phenyl-4-arsonic acid)glycine-4′,1′-hydroxynaphthalide, or *N-(Phenyl-4-arsonic acid)glycyl-4′-amino-1′-naphthol*.—From 4-chloro-

acetylamino-1-naphthol as indicated above. It is purified through the sodium salt, yielding microscopic crystals containing approximately 1.5 molecules of water of crystallization, and are practically insoluble in boiling water, sparingly soluble in alcohol, and readily in hot methyl alcohol. The anhydrous substance darkens above 200° and decomposes at 240-2°.[1066]

N-(Phenyl-4-arsonic acid)glycyl-4′-aminopyrocatechol, [N-(Phenyl-4-arsonic acid)glycine-3′,4′-dihydroxyanilide],

$$H_2O_3AsC_6H_4NHCH_2CONHC_6H_3(OH)_2.$$

On boiling atoxyl with 4-chloroacetylaminopyrocatechol there are obtained faintly pink, glistening leaflets which on rapid heating blacken above 200° and decompose at about 260-5°. It is soluble in hot 50 per cent alcohol, very sparingly in hot ethyl or methyl alcohol, but difficultly in boiling water, separating on cooling as long, narrow, lustrous plates. When dissolved in an excess of dilute sodium hydroxide solution it rapidly turns deep orange in color, while ferric chloride added to an aqueous solution of the acid causes a bluish-purple coloration.[1067]

N-(Phenyl-4-arsonic acid)glycyl-3′-amino-6′-bromophenol,

$$H_2O_3AsC_6H_4NHCH_2CONHC_6H_3{<}\begin{matrix}Br\\OH\end{matrix},$$

is made from 2-bromo-5-chloroacetylaminophenol as above, yielding lustrous leaflets which decompose at 255° with preliminary sintering, and are very sparingly soluble in boiling water, methyl or ethyl alcohol.[1067]

N-(Phenyl-4-arsonic acid)glycyl-3′-amino-4′,6′-dichlorophenol,

$$H_2O_3AsC_6H_4NHCH_2CONHC_6H_2Cl_2(OH),$$

from 2,4-dichloro-5-chloroacetylaminophenol by the usual sodium iodide—50 per cent alcohol method, forms flat, colorless, microscopic needles which begin to darken at about 220°, but melt and decompose at about 280°. It is practically insoluble in boiling water or 50 per cent alcohol.[1066]

N-(Phenyl-4-arsonic acid)glycine-p′-anisidide,

$$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4OCH_3,$$

formed in the usual manner from chloroacetyl-p-anisidine in the presence of sodium iodide, is isolated through its sodium salt as lustrous leaflets which darken and soften at about 230°. It is practically in-

soluble in boiling water or 50 per cent alcohol, and gives a flesh-colored solution with concentrated sulfuric acid.[1065]

N-(Phenyl-4-arsonic acid)glycyl-3'-aminophenoxyacetic acid,

$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4OCH_2COOH$.

From m-chloroacetylaminophenoxyacetic acid without the aid of sodium iodide. It forms radiating masses of microcrystals containing about one molecule of water of crystallization, and fairly easily soluble in boiling water or 50 per cent alcohol. When rapidly heated the anhydrous substance softens at 180-90°, then darkens and finally decomposes at 250-60°.[1068]

N-(Phenyl-4-arsonic acid)glycyl-4'-aminophenoxyacetic acid is prepared like its meta isomer as a colorless powder which may be converted into aggregates of flat, microscopic needles and platelets darkening at 250° but remaining unmelted below 285°. It is appreciably soluble in boiling 50 per cent alcohol, but practically insoluble in hot water, methyl or ethyl alcohol. Its sodium salt consists of glistening, microscopic leaflets, containing three molecules of water of crystallization.[1068]

N-(Phenyl-4-arsonic acid)glycyl-3'-methyl-4'-aminophenoxyacetic acid, $H_2O_3AsC_6H_4NHCH_2CONHC_6H_3(CH_3)OCH_2COOH$, made from atoxyl and 3-methyl-4-chloroacetylaminophenoxyacetic acid, is finally isolated as warty aggregates of microscopic needles decomposing at 270° with preliminary darkening. It is appreciably soluble in methyl alcohol or boiling water, and readily in hot methyl or ethyl alcohol. The sodium salt forms well-defined needles easily soluble in water.[1069]

N-(Phenyl-4-arsonic acid)glycyl-2'-aminophenoxyacetamide,

$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4OCH_2CONH_2$,

is made from o-chloroacetylaminophenoxyacetamide, forming a voluminous mass of microscopic needles containing one molecule of water of crystallization. The acid is very sparingly soluble in boiling water, and somewhat more so in hot 50 per cent alcohol. When anhydrous it decomposes at about 280° with preliminary darkening.[1070]

N-(Phenyl-4-arsonic acid)glycyl-4'-aminophenoxyacetamide. — In this case p-chloroacetylaminophenoxyacetamide and sodium iodide are employed, the acid separating as sheaves and plumes of minute, flat needles very sparingly soluble in boiling water or 50 per cent alcohol, and not melting below 280°. Its sodium salt forms long, flat, microscopic needles containing five molecules of water of crystallization.[1071]

N-(Phenyl-4-arsonic acid)glycyl-4'-aminophenoxyacetylurea,

$$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4OCH_2CONHCONH_2,$$

derived from p-chloroacetylaminophenoxyacetylurea, and purified through the sodium salt, forms microscopic needles containing $\frac{1}{2}H_2O$. The anhydrous acid slowly decomposes at about 290° with preliminary darkening, and is very difficultly soluble in boiling water or 50 per cent alcohol. Its sodium salt contains four molecules of water of crystallization.[1071]

N-(Phenyl-4-arsonic acid)glycyl-anthranilic acid,

$$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4COOH,$$

is made by saponifying its ethyl ester with dilute caustic soda at ordinary temperature. Characteristic octahedra decomposing at 230-5° with preliminary softening and darkening, practically insoluble in boiling water, appreciably soluble in boiling methyl or ethyl alcohol or 50 per cent alcohol.[1072]

N-(Phenyl-4-arsonic acid)glycyl-anthranilic ethyl ester, prepared from chloroacetylanthranilic ethyl ester in the presence of sodium iodide, crystallizes from 50 per cent alcohol in rosets of delicate needles which do not decompose below 280°, and are readily soluble in hot methyl or ethyl alcohol.[1072]

N-(Phenyl-4-arsonic acid)glycyl-2'-aminobenzamide,

$$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4CONH_2.$$

From o-chloroacetylaminobenzamide by the sodium iodide-alcohol method. Faintly yellow, radiating masses of delicate, microscopic needles containing $1H_2O$. When rapidly heated to 165° and then slowly it sinters and gradually melts at 170°. It is sparingly soluble in cold, readily in hot water or alcohol, and appreciably in cold methyl alcohol. Its sodium salt forms globules of minute, slightly yellow crystals containing $4\frac{1}{2}H_2O$ and readily soluble in water.[1073]

N-(Phenyl-4-arsonic acid)glycyl-3'-aminobenzamide is prepared like the preceding compound, crystallizing from hot 50 per cent alcohol as rosets of microscopic spears containing $2\text{-}2\frac{1}{2}H_2O$, and practically insoluble in boiling water. When rapidly heated it darkens and shows signs of decomposition above 200°, but does not decompose completely until 280°.[1074]

N-(Phenyl-4-arsonic acid)glycyl-4'-aminobenzamide, formed like the preceding two compounds, exists as nodules of microscopic needles which do not melt below 280°. Its sodium salt crystallizes in rosets of

thin, microscopic needles containing 4½ molecules of water of crystallization, and readily dissolving in hot water.[1075]

N-(Phenyl-4-arsonic acid)glycine-3′-carboxamidobenzylamide,

$H_2O_3AsC_6H_4NHCH_2CONHCH_2C_6H_4CONH_2$.

Prepared like the previous compound, employing m-carboxamidochloroacetylbenzylamine. It consists of microscopic needles sparingly soluble in hot water or boiling acetic acid, practically insoluble in boiling alcohol, and decomposing at 237-9° with preliminary darkening. On continued washing with water it tends to become colloidal. The sodium salt crystallizes with $5H_2O$, and is freely soluble in water.[1076]

N-(Phenyl-4-arsonic acid)-α-phenylglycine-3′-carbamidoanilide,

$H_2O_3AsC_6H_4NHCH(C_6H_5)CONHC_6H_4CONH_2$.

From m-phenylchloroacetylaminobenzamide as microcrystals which darken and soften slightly above 250°, melt with effervescence at 261-2°, and are practically insoluble in boiling water or 50 per cent alcohol.[1077]

N-(Phenyl-4-arsonic acid)glycyl-5′-aminosalicylamide,

$H_2O_3AsC_6H_4NHCH_2CONHC_6H_3(OH)CONH_2$,

from 5-chloroacetylaminosalicylamide by the sodium iodide method, yields glistening scales containing one molecule of water of crystallization. When rapidly heated the anhydrous substance softens above 190° and gradually decomposes until fluid at about 255°. It is very sparingly soluble in boiling water or 50 per cent alcohol, the resulting solutions giving a brownish purple coloration with ferric chloride. In alkaline solution it couples with diazotized sulfanilic acid.[1075]

N-(Phenyl-4-arsonic acid)glycyl-3′-aminobenzoylurea,

$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4CONHCONH_2$,

is similarly prepared from m-chloroacetylaminobenzoylurea, and is isolated through its sodium salt as sheaves and plumes of microscopic needles which decompose at about 280° with preliminary darkening and sintering, and are practically insoluble in boiling water or 50 per cent alcohol. Its sodium salt consists of thick, colorless masses of delicate microscopic hairs containing $8H_2O$.[1074]

N-(Phenyl-4-arsonic acid)glycine-3′-carboxureidobenzylamide,

$H_2O_3AsC_6H_4NHCH_2CONHCH_2C_6H_4CONHCONH_2$.

From atoxyl and m(ω-chloroacetylaminomethyl)benzoylurea. Glistening, microscopic aggregates of delicate needles decomposing at 239-40°, and practically insoluble in the usual neutral solvents.[1058]

N-(Phenyl-4-arsonic acid) glycyl-4'-aminoacetophenone,

$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4COCH_3$.

From p-chloroacetylaminoacetophenone by the sodium iodide method. The acid separates from hot, dilute solutions of its salts on addition of acetic acid as long, fine hairs which do not melt below 280°. It is almost insoluble in boiling water, sparingly soluble in hot 50 per cent alcohol, and dissolves in concentrated sulfuric acid with a yellow color.[1078]

N-(Phenyl-4-arsonic acid) glycyl-4'-aminobenzenesulfonic acid,

$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4SO_3H$,

from atoxyl and sodium chloroacetylsulfanilate, forms flat needles containing two molecules of water of crystallization, and is readily soluble in hot, less in cold water, sparingly in alcohol or 10 per cent hydrochloric acid, and practically insoluble in acetone. The anhydrous substance slowly softens and decomposes at 245-6°.[1079]

N-(Phenyl-4-arsonic acid) glycyl-4'-amino-6'-hydroxybenzenesulfonic acid, $H_2O_3AsC_6H_4NHCH_2CONHC_6H_3(OH)SO_3H$, is produced by boiling atoxyl and the sodium salt of 4-chloroacetylamino-6-hydroxybenzenesulfonic acid. The acid crystallizes with about 1.5 molecules of water, is fairly readily soluble in water at ordinary temperatures, but, like many other sulfonic acids, is less soluble in dilute hydrochloric acid. It separates from hot water on thorough chilling as microscopic leaflets difficultly soluble in hot acetic acid, methyl or ethyl alcohol. The anhydrous substance softens and darkens above 200°, but does not melt below 275°. In alkaline solution it couples readily with diazotized sulfanilic acid.[1078]

N-(Phenyl-4-arsonic acid) glycyl-3'-aminobenzenesulfonamide,

$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4SO_2NH_2$,

is prepared by the usual sodium iodide method, employing m-chloroacetylaminobenzenesulfonamide. The product consists of flat, glistening, microscopic needles, often grouped in rosets, which are decomposed at about 265° with preliminary darkening and dissolve in boiling water or 50 per cent alcohol with difficulty.[1079]

N-(Phenyl-4-arsonic acid) glycyl-4'-aminobenzenesulfonamide, made in a similar manner, forms aggregates of thin microscopic leaflets and needles which are insoluble in boiling water or 50 per cent alcohol. On rapid heating it sinters slightly, but does not melt below 280°.[1078]

N-(Phenyl-4-arsonic acid)glycyl-4′-aminophenylacetic acid,

$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4CH_2COOH$,

is produced from atoxyl and p-chloroacetylaminophenylacetic acid as practically colorless, microscopic globules. The dried acid gradually darkens on heating, finally melting and decomposing at 280°. The anhydrous substance is pale yellow, losing its color without dissolving when boiled with water. It is quite soluble in boiling 85 per cent alcohol or methyl alcohol, but only sparingly so in boiling acetic acid.[1080]

N-(Phenyl-4-arsonic acid)glycyl-3′-aminophenylacetamide,

$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4CH_2CONH_2$,

is obtained by the above method from m-chloroacetylaminophenylacetamide as masses of microscopic needles which darken slightly above 220°, decompose at 275-80°, and are soluble in boiling water or 50 per cent alcohol.[1075]

N-(Phenyl-4-arsonic acid)glycyl-4′-aminophenylacetamide, similarly prepared, forms plumes of microscopic hairs sparingly soluble in boiling water or 50 per cent alcohol, and does not melt below 280°. It is very sensitive to fixed alkali because of the aliphatic amide linking. The sodium salt separates as glistening platelets which, after air drying, contain 2.5 molecules of water of crystallization, and dissolve readily in water.[1080]

N-(Phenyl-4-arsonic acid)-α-phenylglycyl-4′-aminophenylacetamide,

$H_2O_3AsC_6H_4NHCH(C_6H_5)CONHC_6H_4CH_2CONH_2$,

made from α-phenylchloroacetyl-p-aminophenylacetamide, crystallizes in minute plates and flat needles with 0.5 molecule of water of crystallization, and is sparingly soluble in boiling water, more easily in boiling 50 per cent alcohol. When anhydrous it turns yellow and softens on heating, melting with decomposition at 222-3°.[1077]

N-(Phenyl-4-arsonic acid)glycyl-4′-aminophenylacetureide,

$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4CH_2CONHCONH_2$.

From p-chloroacetylaminophenylacetylurea are obtained plumes of minute hairs which darken slightly without melting below 280°, and are almost insoluble in boiling water or 50 per cent alcohol. Its sodium salt separates as microscopic, hexagonal plates containing three molecules of water of crystallization.[1070]

N-(Phenyl-4-arsonic acid)glycineureide,

$H_2O_3AsC_6H_4NHCH_2CONHCONH_2$,

separates on refluxing atoxyl with chloroacetylurea for 15 minutes and further heating on the water-bath as aggregates of microscopic needles

sparingly soluble in boiling water or 50 per cent alcohol, and almost insoluble in methyl alcohol. When rapidly heated it sinters slightly above 230° and darkens, but does not melt below 280°.

The sodium salt is obtained as well-defined, hexagonal or diamond-shaped, microscopic platelets by adding a saturated sodium acetate solution to a neutral solution of the acid. When air-dried it contains two molecules of water of crystallization, and is readily soluble in water, the resulting solution yielding precipitates with salts of the heavy metals. The silver salt forms colorless, microscopic needles, while magnesia mixture precipitates the magnesium salt only on boiling.[1081]

α-N(Phenyl-4-arsonic acid)aminopropionylurea,

$$H_2O_3AsC_6H_4NHCH(CH_3)CONHCONH_2,$$

prepared by boiling p-arsanilic acid in sodium hydroxide solution with α-bromopropionylurea for one hour, crystallizes from 50 per cent alcohol in aggregates of minute needles sparingly soluble in water or methyl alcohol. When rapidly heated to 220°, then slowly, it decomposes at 225-6°.[1082]

N-(Phenyl-4-arsonic acid)-α-phenylglycineureide,

$$H_2O_3AsC_6H_4NHCH(C_6H_5)CONHCONH_2,$$

similarly prepared from phenylchloroacetylurea, separates as radiating masses of microscopic needles containing one molecule of water of crystallization, soluble in boiling water or 50 per cent alcohol, but sparingly so in cold. When rapidly heated the anhydrous substance swells and evolves gas at 195-7°.[1048]

N-(Phenyl-4-arsonic acid)glycine-methylureide,

$$H_2O_3AsC_6H_4NHCH_2CONHCONHCH_3,$$

is derived from atoxyl by boiling with α-chloroacetyl-β-methylurea for one hour, and purifying through the sodium salt. The substance is sparingly soluble in hot water, separating on cooling as long, thin, glistening needles decomposing at 224-5°. It is also difficultly soluble in boiling 50 per cent alcohol, and practically insoluble in the usual organic solvents.

The sodium salt crystallizes as microscopic platelets containing seven molecules of water of crystallization, and is quite readily soluble in water, especially on warming. The solution of the sodium salt yields a precipitate with magnesia mixture only on boiling; other heavy metal salts readily produce insoluble precipitates, the silver salt separating as thin, microscopic platelets.[1083]

N-(Phenyl-4-arsonic acid)glycine-ethylureide,

$H_2O_3AsC_6H_4NHCH_2CONHCONHC_2H_5$.

From α-chloroacetyl-β-ethylurea as in the case of methylureide. The substance is precipitated from the hot solution of its sodium salt by acetic acid as plumes of microscopic needles which are very difficultly soluble in hot water or methyl alcohol, but more readily so in 50 per cent alcohol. When rapidly heated to 220°, then slowly, it decomposes at 223-5°.

The sodium salt separates on treating a carefully neutralized solution of the acid with alcohol in thin microscopic platelets, which when recrystallized from hot 85 per cent alcohol contain about 4.5 molecules of water of crystallization, and dissolve readily in water.[1083]

N-(Phenyl-4-arsonic acid)glycine-phenylureide,

$H_2O_3AsC_6H_4NHCH_2CONHCONHC_6H_5$,

is obtained by boiling an alkaline solution of p-arsanilic acid with chloroacetylphenylurea, sodium iodide and alcohol for four hours. Feathery aggregates of silky hairs, appreciably soluble in boiling 50 per cent alcohol, from which it separates on cooling as long, fine needles. It is almost insoluble in boiling water or methyl alcohol, and melts at 280° with slight preliminary darkening. The sodium salt consists of lustrous leaflets, but when recrystallized from 50 per cent alcohol, flat needles containing $5H_2O$, are obtained.[1084]

N-(Phenyl-4-arsonic acid)glycine-benzylureide,

$H_2O_3AsC_6H_4NHCH_2CONHCONHCH_2C_6H_5$,

prepared by boiling p-arsanilic acid dissolved in N-sodium hydroxide solution, α-chloroacetyl-β-benzylurea, and a little alcohol for three hours, crystallizes from 50 per cent alcohol in rosets of delicate needles, which when rapidly heated to 220°, then slowly, decompose at 225°. It is sparingly soluble in boiling water, and practically insoluble in methyl alcohol.[1082]

N-(Phenyl-4-arsonic acid)glycine-4′-acetylaminophenylureide,

$H_2O_3AsC_6H_4NHCH_2CONHCONHC_6H_4NHCOCH_3$.

From atoxyl, alcohol p-acetylaminophenylchloroacetylurea and sodium iodide as above, separating in clusters of flat, microscopic needles which decompose at 265-6° with preliminary sintering and darkening. The acid is almost insoluble in boiling water but is appreciably soluble in hot 50 per cent alcohol, separating on cooling as plumes of long, delicate hairs. The sodium salt consists of masses of flat needles containing five molecules of water of crystallization.[1084]

N-(Phenyl-4-arsonic acid)glycine-3'-oxamylaminophenylureide,

$H_2O_3AsC_6H_4NHCH_2CONHCONHC_6H_4NHCOCONH_2$.

Produced as above by employing m-chloroacetyluraminooxanilamide. It consists of a microcrystalline powder almost insoluble in boiling water, and appreciably in hot 50 per cent alcohol. When rapidly heated it decomposes at 223-4°.[1085]

N-(Phenyl-4-arsonic acid)glycine-4'-hydroxyphenylureide,

$H_2O_3AsC_6H_4NHCH_2CONHCONHC_6H_4OH$,

similarly formed from p-acetoxyphenylchloroacetylurea, is isolated through its sodium salt as microscopic needles containing 1.5 molecules of water of crystallization. The anhydrous substance darkens above 200°, sinters and chars at about 250°, but does not melt up to 280°. The sodium salt crystallizes from 50 per cent alcohol in glistening leaflets containing $4\text{-}4\frac{1}{2}H_2O$, and is fairly readily soluble in water, particularly on warming.[1085]

N-(Phenyl-4-arsonic acid)glycyl-4'-uraminophenoxyacetamide,

$H_2O_3AsC_6H_4NHCH_2CONHCONHC_6H_4OCH_2CONH_2$.

In this case p-chloroacetyluraminophenoxyacetamide is employed. The acid, isolated through its sodium salt, consists of glistening, diamond-shaped platelets almost insoluble in boiling water or 50 per cent alcohol. When rapidly heated it decomposes at 243-4° with preliminary sintering and darkening. The sodium salt crystallizes from 50 per cent alcohol in aggregates of slightly purplish plates which are fairly soluble in water, especially on warming.[1086]

N-(Phenyl-4-arsonic acid)glycyl-3'-uraminobenzamide,

$H_2O_3AsC_6H_4NHCH_2CONHCONHC_6H_4CONH_2$.

From m-chloroacetyluraminobenzamide by boiling for two hours. The acid separates as a rather voluminous, micro-crystalline powder, very sparingly soluble in boiling water, but somewhat more soluble in boiling 50 per cent alcohol, from which it separates as sheaves of flat, microscopic needles. When rapidly heated it melts at 213-4° with effervescence and darkening.[1086]

N-(Phenyl-4-arsonic acid)glycyl-4'-uraminobenzamide.—For the production of this compound p-chloroacetyluraminobenzamide is employed, and the boiling continued for 5 hours. It consists of short, microscopic needles decomposing at 245° with preliminary darkening.[1087]

N-(Phenyl-4-arsonic acid)glycyl-3′-uraminophenylacetamide,

$$H_2O_3AsC_6H_4NHCH_2CONHCONHC_6H_4CH_2CONH_2.$$

Similarly prepared by boiling the reaction mixture containing m-chloroacetyluraminophenylacetamide for three hours. It crystallizes from hot water in felted needles soluble in 50 per cent alcohol and decomposing, when rapidly heated, at 214-6°.[1087]

N-(Phenyl-4-arsonic acid)glycyl-4′-uraminophenylacetamide.—In this case p-chloroacetyluraminophenylacetamide is used, and the mixture boiled for two hours. The acid is isolated through its sodium salt as plumes of delicate needles containing $1H_2O$ and very sparingly soluble in boiling water, though more readily so in boiling 50 per cent alcohol. When rapidly heated the anhydrous substance decomposes at 218-21°.

Its sodium salt is salted out of solution with sodium acetate, and separates from alcohol-water as microscopic, hexagonal platelets containing about 2.5 molecules of water of crystallization.[1087]

N-(Phenyl-4-arsonic acid)glycyl-N-methylanthranilic acid,

$$H_2O_3AsC_6H_4NHCH_2CON(CH_3)C_6H_4COOH,$$

is best obtained by first preparing the corresponding ethyl ester and then hydrolyzing as above. It consists of microscopic aggregates of needles or short, flat plates which darken and decompose at 230°, are very difficultly soluble in boiling water or methyl alcohol, but more readily soluble in hot 50 per cent alcohol, from which it can be recrystallized.[1072]

N-(Phenyl-4-arsonic acid)glycine dimethylamide,

$$H_2O_3AsC_6H_4NHCH_2CON(CH_3)_2,$$

consists of thin, microscopic needles, and is prepared by boiling p-arsanilic acid with chloroacetyldimethylamine. The substance is very sparingly soluble in the neutral solvents, and, when rapidly heated, decomposes at 241-2°.[1088]

N-(Phenyl-4-arsonic acid)glycine diethylamide,

$$H_2O_3AsC_6H_4NHCH_2CON(C_2H_5)_2,$$

is prepared as above from arsanilic acid and chloroacetyldiethylamine, forming microscopic aggregates of short needles which are difficultly soluble in boiling water, but readily in boiling methyl or 50 per cent ethyl alcohol. When rapidly heated it sinters and darkens above 195°, and melts at 199-201° with gas evolution.[1088]

N-(Phenyl-4-arsonic acid)glycine piperidide,

$$H_2O_3AsC_6H_4NHCH_2CONC_5H_{10},$$

is formed as above, employing chloroacetylpiperidine. It crystallizes from hot 50 per cent alcohol in characteristic sheaves of thin, micro-

scopic needles decomposing at 218-21° with preliminary softening and darkening. The acid is soluble in hot methyl or 50 per cent ethyl alcohol, but very sparingly so in hot water.[1088]

Phenacyl-p-arsanilic acid, $H_2O_3AsC_6H_4NHCH_2COC_6H_5$.—In this case ω-bromoacetophenone is used, the compound being finally obtained as faintly yellow, arborescent aggregates of delicate, microscopic needles decomposing at 185-7° with preliminary softening. It is only sparingly soluble in the usual solvents, but dissolves more readily in alkalis or concentrated sulfuric acid.[1089]

2′-Hydroxy-5′-acetylaminophenacyl-p-arsanilic acid,

$$H_2O_3AsC_6H_4NHCH_2COC_6H_3\begin{matrix} \diagup OH \\ \diagdown NHCOCH_3 \end{matrix}$$

From p-arsanilic acid and 3-acetylamino-6-hydroxyphenacylbromide. A dark yellow powder consisting of aggregates of microscopic platelets which redden and decompose at 228°, dissolve in concentrated sulfuric acid with a reddish-brown color, and are practically insoluble in hot water or 50 per cent alcohol.[1090]

4-Methylaminophenylarsonic acid, $H_2O_3AsC_6H_4NHCH_3$, may be prepared by diazotizing 4-aminomethylacetanilide by Bart's method and subsequently saponifying;[1091] by oxidizing the corresponding arsineoxide with hydrogen peroxide in the presence of caustic soda,[1092] or by condensing methylaniline with arsenic trichloride in pyridine medium at 106-8° for two hours, and oxidizing the resulting dichloroarsine with hydrogen peroxide in either acid or alkaline solution. In this case, however, more or less of the secondary compound,

$$(CH_3.NH.C_6H_4)_2AsO.OH,$$

is formed at the same time, and is separated by dissolving in an alcohol-ether mixture in which the primary acid is insoluble.[1093] The arsonic acid consists of leaflets readily soluble in water, alcohol or dilute acetic acid, and decomposing at 190°. With silver nitrate it forms a silver salt, $CH_3NH.C_6H_4AsO(OAg)_2$, a white crystalline powder soluble in ammonia or nitric acid, and darkening on exposure to light.

The corresponding *ethyl* and *amyl aminophenylarsonic acids* have also been prepared starting with the alkylaniline as above. The amyl derivative consists of colorless lamellæ decomposing at 172°.[1093]

Benzyl-p-arsanilic acid, $C_6H_5CH_2NHC_6H_4AsO_3H_2$, is formed on refluxing atoxyl, benzyl chloride, sodium iodide and alcohol, separating

as flat, lustrous, microscopic needles. It crystallizes from hot 50 per cent alcohol as arborescent masses of micro-crystals and larger prisms, decomposing at about 255°, readily soluble in methyl alcohol, strong hydrochloric acid, boiling alcohol or acetic acid, sparingly in hot water, and insoluble in 10 per cent hydrochloric acid. On adding sodium nitrite to a hot acetic acid solution of the compound, yellow spherules of microscopic crystals, presumably the nitroso compound, separate on cooling and rubbing. The sodium salt consists of glistening platelets readily soluble in water.[1129]

4'-Nitrobenzyl-p-arsanilic acid, $H_2O_3AsC_6H_4NHCH_2C_6H_4NO_2$, separates on boiling atoxyl, p-nitrobenzylchloride and alcohol in the form of sheaves of flat, yellow, microscopic needles which do not melt up to 280°. It is almost insoluble in boiling water, and only sparingly soluble in boiling methyl alcohol, acetic acid or 85 per cent alcohol.[1095]

4'-Aminobenzyl-p-arsanilic acid, $H_2O_3AsC_6H_4NHCH_2C_6H_4NH_2$, produced by reducing the preceding nitro compound with ferrous hydroxide, consists of colorless aggregates of microscopic leaflets decomposing at about 202°, and practically insoluble in hot water or 50 per cent alcohol. On boiling its dilute ammoniacal solution there is precipitated a white, amorphous alteration product which is not obtained with fixed alkali. The pure acid is soluble in both alkali and mineral acids, a solution in the latter being readily diazotizable, coupling with R-salt to form a deep red dye.[1095]

4'-Carboxybenzyl-p-arsanilic acid, $H_2O_3AsC_6H_4NHCH_2C_6H_4COOH$, results from the interaction of p-carboxybenzyl chloride and atoxyl, finally crystallizing as delicate, microscopic needles which do not melt below 280°, are sparingly soluble in hot 50 per cent alcohol or acetic acid, and insoluble in the other neutral solvents. Its sodium salt consists of aggregates of flat needles containing about 0.5 molecule of water of crystallization.[1096]

4'-Carboxamidobenzyl-p-arsanilic acid,

$$H_2O_3AsC_6H_4NHCH_2C_6H_4CONH_2.$$

Sheaves and plumes of microscopic needles prepared from atoxyl and p-(ω-chloromethyl) benzamide. The acid does not melt below 280°, and is almost insoluble in boiling water, 50 per cent alcohol or methyl alcohol. Its sodium salt crystallizes with 2.5 molecules of water as aggregates of thin plates easily soluble in water.[1096]

3′-Nitro-4′-hydroxybenzyl-p-arsanilic acid,

$$H_2O_3AsC_6H_4NHCH_2C_6H_3(OH)(NO_2),$$

is obtained from atoxyl and 3-nitro-4-hydroxybenzyl chloride in alcohol medium, and separates from 85 per cent alcohol as minute, yellow crystals containing one molecule of water of crystallization. When rapidly heated the anhydrous substance darkens and sinters above 210°, and decomposes at about 245-50°; it is practically insoluble in boiling water, sparingly in cold acetic acid, methyl or ethyl alcohol and readily on boiling.[1095]

3′-Amino-4′-hydroxybenzyl-p-arsanilic acid,

$$H_2O_3AsC_6H_4NHCH_2C_6H_3(OH)(NH_2),$$

from the preceding compound by reduction with ferrous hydroxide, forms almost colorless, microscopic platelets containing 0.5 molecule of water of crystallization. It is sparingly soluble in boiling water or 50 per cent alcohol, and does not melt below 285°.[1097]

Phenoxyethyl-p-arsanilic acid, $C_6H_5OCH_2CH_2NHC_6H_4AsO_3H_2$, is obtained by boiling atoxyl, phenoxyethyl bromide, sodium iodide and alcohol, the acid separating as glistening scales containing $1H_2O$, very sparingly soluble in boiling water or acetic acid, appreciably so in hot methyl or ethyl alcohol, and remaining undecomposed below 280° when anhydrous. The sodium salt crystallizes with 3.5 molecules of water as flat, microscopic needles.[1098]

4′-Acetylaminophenoxyethyl-p-arsanilic acid,

$$CH_3CONHC_6H_4OCH_2CH_2NHC_6H_4AsO_3H_2.$$

p-Arsanilic acid is condensed as in the previous example with p-acetylaminophenoxyethyl bromide to form delicate, glistening needles and platelets which do not melt below 275°. It is practically insoluble in boiling water, very difficultly soluble in hot methyl or ethyl alcohol, but dissolves in hot 50 per cent alcohol or glacial acetic acid. The sodium salt crystallizes with about 3 molecules of water as colorless microscopic platelets.[1098]

2′-Carboxamidophenoxyethyl-p-arsanilic acid,

$$H_2O_3AsC_6H_4NHCH_2CH_2OC_6H_4CONH_2,$$

is made from salicylamidebromoethyl ether (2-bromoethoxybenzamide), crystallizing in wedge-shaped, microscopic prisms very difficultly soluble in boiling water, and sparingly in most hot solvents except hot acetic acid or 50 per cent alcohol. It melts on prolonged heating at 280°, but not below this temperature.[1089]

N-(Phenyl-4-arsonic acid)acetylglycine,

$$H_2O_3AsC_6H_4N(COCH_3)(CH_2COOH),$$

is prepared by condensing arsenic trichloride with acetylanilinoacetonitrile, $C_6H_5N\begin{matrix} \diagup COCH_3 \\ \diagdown CH_2CN \end{matrix}$, oxidizing the resulting dichloroarsine to the arsonic acid, and finally saponifying the nitrile group.[611]

Amyl ester of N-(phenyl-4-arsonic acid)nitrosoglycine,

$$H_2O_3AsC_6H_4N(NO)CH_2CO_2C_5H_{11},$$

is prepared by treating a solution of the amyl ester of N-(phenyl-4-arsonic acid)methylglycine in 70 per cent sulfuric acid with a solution of sodium nitrite in the same solvent at 0°. The substance is colorless, insoluble in water or mineral acids, soluble in acetic acid, and more so in alcohol or dilute alkalis. It decomposes with evolution of gas at 150°, and evolves nitric oxide when copper powder is added to its solution in fairly concentrated sulfuric acid.[1099]

N-(Phenyl-4-arsonic acid)nitrosoglycineamide,

$$H_2O_3AsC_6H_4N(NO)CH_2CONH_2,$$

results upon treating an aqueous solution of the sodium salt of N-(phenyl-4-arsonic acid)glycineamide with sodium nitrite and hydrochloric acid. It forms rosets and sheaves of silky needles which intumesce at 182-3°, and are readily soluble in hot water, acetic acid, methyl or ethyl alcohol. Under sulfuric acid it turns yellow, dissolving to an almost colorless solution giving a brown-red Liebermann test.[1045]

N-(Phenyl-4-arsonic acid)nitrosoglycineanilide,

$$H_2O_3AsC_6H_4N(NO)CH_2CONHC_6H_5,$$

is produced by the action of sodium nitrite upon a glacial acetic acid suspension of N-(phenyl-4-arsonic acid)glycineanilide. It separates as sheaves of long, flat, colorless needles containing $1H_2O$, effervescing at 190-2°, very sparingly soluble in boiling water, sparingly in cold 95 per cent alcohol, readily in boiling 50 per cent alcohol and quite easily in acetic acid. It is turned brown by sulfuric acid, but dissolves to a colorless solution; in the presence of phenol, however, a brown solution is obtained, changing rapidly to deep green.[1051]

N-4-Nitroso methylaminophenylarsonic acid,

$$H_2O_3AsC_6H_4N(CH_3)(NO),$$

may be produced by treating p-dimethylaminophenylarsonic acid, dissolved in moderately strong sulfuric acid, with a solution of sodium

nitrite at 0°,[1099] or by introducing the nitroso group into N-4-methylaminophenylarsonic acid.[1091] It consists of white needles decomposing at 182-90°, and difficultly soluble in alcohol or acetic acid. On warming with strong hydrochloric acid the nitroso group is split off.

N-4-Acetyl methylaminophenylarsonic acid,

$$H_2O_3AsC_6H_4N(CH_3)(OCCH_3),$$

is obtained by the method indicated under methylarsanilic acid. It is a white crystalline powder, soluble in hot alcohol or water, and melting with sintering at 195°. It can be saponified with dilute alkalis to methylarsanilic acid.[1091]

N-(Phenyl-4-arsonic acid)methylglycine,

$$H_2O_3AsC_6H_4N(CH_3)CH_2COOH,$$

as well as the *corresponding ethyl* and *amyl* derivatives, are obtained by the hydrolysis of their esters with caustic soda. The first mentioned is a white crystalline powder which evolves carbon dioxide at higher temperatures, yielding 4-dimethylaminophenylarsonic acid.

The esters just referred to may be obtained by reacting N-phenylalkylglycine esters with arsenic trichloride or bromide in a pyridine medium at 108-10°, and oxidizing the resulting products with hydrogen peroxide in aqueous solution. In this way the *ethyl, propyl* and *amyl esters* of *N-(phenyl-4-arsonic acid)methylglycine* and *ethyl* and *amyl esters* of *N-(2-methylphenyl-4-arsonic acid)methylglycine* have been prepared. The *propyl ester of N-(phenyl-4-arsonic acid)methylglycine,* $H_2O_3AsC_6H_4N(CH_3)CH_2COOC_3H_7$, is a white crystalline mass melting at 153-4° and blackening at 190°. It is sparingly soluble in water, ether or mineral acids, but more so in alcohol, acetone or acetic acid.[1100, 1101]

4-Dimethylaminophenylarsonic acid, $(CH_3)_2NC_6H_4AsO(OH)_2$, may be formed from p-arsanilic acid by heating with an excess of dimethylsulfate, adding an excess of caustic soda to the product, and precipitating with acetic acid;[1102] also by oxidizing dimethylaminophenylarsineoxide either with a slight excess of mercuric oxide in aqueous suspension[1103] or with hydrogen peroxide in alkali medium. In the latter case it is not essential to isolate the oxide, it being merely necessary to condense dimethylaniline with arsenic trichloride and add caustic soda until the precipitated oxide is redissolved.[1104]

The acid separates in long, colorless leaflets sparingly soluble in alcohol or water, more so in hot water, alcohol or dilute acetic acid, and readily in dilute mineral acids or alkalis. On heating it gradually

decomposes without melting. Its monosodium salt crystallizes with five molecules of water in the form of shiny leaflets.

11. *Di- and Triamino Aryl Arsonic Acids.*—The preparation of arsonic acids containing more than one amino group in the nucleus may be effected by mildly reducing the corresponding nitroamino derivatives. The reagents employed are sodium hydrosulfite at low temperature, ferrous chloride or sulfate in alkaline medium, or hydrogen under pressure in the presence of palladous hydroxide as a catalyst. They may also be obtained by oxidizing the corresponding tetraamino arseno compounds.

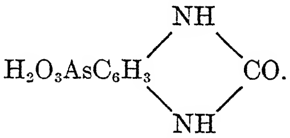
The products are crystalline substances soluble in dilute alkalis or mineral acids, methyl alcohol, acetic acid or hot water, sparingly in ethyl alcohol or cold water, and insoluble in the other organic solvents. They are less stable than the monoamino acids—their alkaline solutions oxidize more rapidly on exposure to air, and also reduce ammoniacal silver solutions. The 3,4-diaminophenyl- and the 5,6-diamino-3-methylphenylarsonic acids give characteristic deep violet colorations with potassium bichromate solution in the presence of dilute hydrochloric acid. It is interesting to note that on diazotizing 2,5-diaminophenylarsonic acid, only one amino group is affected, and that the diazo group may be replaced by hydrogen, yielding m-arsanilic acid. On the other hand, the 3,4-diamino acid cannot be diazotized, forming diazimidophenylarsonic acid with one mole of nitrous acid at 0°.

The N-substituted derivatives are made either directly from the amino acids or by reducing the corresponding nitro acids.

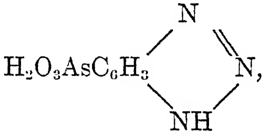
2,3-Diaminophenylarsonic acid, $H_2O_3AsC_6H_3(NH_2)_2$, may be obtained as lustrous leaflets, m. p. 205-8°, when the 2-nitro-3-amino acid is mildly reduced with sodium hydrosulfite at ordinary temperature, and the resulting product recrystallized from water.[724]

3,4-Diaminophenylarsonic acid is prepared by the reduction of an alkaline solution of the corresponding nitro amino acid with either sodium hydrosulfite at 0°,[1105] or with hydrogen under pressure, palladous hydroxide being used as a catalyzer.[901] It crystallizes from hot water in colorless prisms containing $\frac{1}{2}H_2O$, darkening at 140° and melting with decomposition at 158-9°. The compound is readily soluble in acids, alkalis, hot water, methyl alcohol, glacial or 50 per cent acetic acid, sparingly in cold water or alcohol, insoluble in acetone or ether, and reduces ammoniacal silver solution. Its acid solution gives a deep violet color with a drop of potassium bichromate, while its alkaline solution darkens on standing in air. It behaves like a typical ortho diamine, yielding a diazimine with nitrous acid, a carbamide derivative with phosgene and an azine with phenanthraquinone.

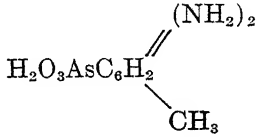
o-Phenyleneurearsonic acid (*Benzimidoazolonearsonic acid*),



Prisms or platelets not melting at 300°, and only slightly soluble in water or the usual solvents. It is formed by treating a solution of 3,4-diaminophenylarsonic acid in dilute soda with a solution of phosgene in toluene, extracting with ether and acidifying.[1106]

Diazoimidophenylarsonic acid,  made by treating a hydrochloric acid solution of 3,4-diaminophenylarsonic acid with one molecular proportion of sodium nitrite at 0°, crystallizes as colorless prisms carbonizing above 300°, soluble in alkalis, concentrated mineral acids, hot water, 50 per cent acetic acid, methyl or ethyl alcohol but only sparingly so in glacial acetic acid, acetone or ether. It forms no dyes with azo components.[1107]

2,5-Diaminophenylarsonic acid (*p-Phenylenediaminearsonic acid*).—From 2-amino-5-nitrophenylarsonic acid in alkaline solution by reduction with ferrous chloride at ordinary temperature. It crystallizes as fine needles which turn violet on exposure to air or sunlight, decompose at 210-15°, are sparingly soluble in cold water or alcohol, but readily in hot water, dilute acids, alkalis or sodium acetate solution. On diazotizing, only the amino group in position 2 is affected, the resulting diazo solution coupling readily with resorcinol or β-naphthol but slowly with R-salt. By treating the above diazo solution with alcohol and copper powder, m-arsanilic acid is obtained.[939, 1108]

5,6-Diamino-3-methylphenylarsonic acid,  , is derived from 5-nitro-6-amino-3-methylphenylarsonic acid by reduction with sodium hydrosulfite in alkaline solution at —1°. It crystallizes from water with $1\frac{1}{2}$-$2H_2O$ as colorless needles which slowly decompose on keeping, are fairly readily soluble in methyl alcohol or acetic acid but very sparingly so in ether, benzene or petroleum. Its solution in dilute hydrochloric acid gives a characteristic deep violet coloration with a drop of potassium bichromate solution.[1109]

3,4,5-Triaminophenylarsonic acid, $H_2O_3AsC_6H_2(NH_2)_3$, results upon reducing an alkaline solution of 3,5-dinitro-4-aminophenylarsonic acid with ferrous chloride[1110] or sodium hydrosulfite at 0-5°.[592] It exists as colorless needles which decompose at 170-5°, are practically insoluble in alcohol, water or acetone, difficultly soluble in methyl alcohol, 50% acetic acid or sodium acetate solution, but more easily upon warming, and are readily soluble in dilute mineral acids, alkali hydroxides or carbonates. It can be diazotized to a yellowish diazo compound which couples orange with resorcin and brilliant bluish-red with R-salt. Its alkaline solution yields an unstable red coloration with potassium ferricyanide or sodium hypochlorite; its ammoniacal solution slowly reduces silver nitrate, while its concentrated sulfuric acid solution gives with one drop of nitric acid a brown coloration which rapidly changes to olive green and finally to pure blue.

3-Amino-4-carbethoxyaminophenylarsonic acid,

$$H_2O_3AsC_6H_3(NH_2)(NH.COOC_2H_5),$$

is formed by reducing the corresponding nitrocarbethoxy compound with ferrous sulfate in the presence of an ammoniacal barium hydroxide solution.[822]

3,4-Di(acetylamino)phenylarsonic acid, $H_2O_3AsC_6H_3(NH.COCH_3)_2$, is produced by treating a methyl alcoholic solution of the corresponding diamino arsonic acid with a mixture of acetic acid and acetic anhydride, distilling off the alcohol, and boiling the residual solution. It crystallizes from water as a felted mass of fine needles retaining from 2-2½% of the solvent. On heating with water in a sealed tube at 130° for several hours, 2-methyl-1,3-benzodiazole-5-arsonic acid is formed.[1111]

2,5-Diaminophenylarsonic acid oxanilide,

$$\begin{array}{l} OC.HNC_6H_3(NH_2)AsO_3H_2 \\ | \\ OC.HNC_6H_3(NH_2)AsO_3H_2 \end{array},$$

is obtained by reducing 5-nitro-2-aminophenylarsonic acid oxanilide with iron powder and dilute acetic acid.[1112]

12. *Halogenated Amino Aryl Arsonic Acids.*—Upon attempting to halogenate the aminoarylarsonic acids directly in aqueous or mineral acid solution, the C-As linkage is destroyed, and the products obtained are trihalogenated amines, arsenic- and haloid acids, e.g.,

$$\begin{array}{l} H_2N.C_6H_4AsO_3H_2 + 3Br_2 + H_2O \longrightarrow \\ H_2N.C_6H_2Br_3 + H_3AsO_4 + 3HBr. \end{array}$$

This decomposition can be almost entirely avoided by treating the above amino acids either with halogens in an anhydrous solvent such

as absolute methyl alcohol or glacial acetic acid, or with nascent halogens derived from sodium hypochlorite, sodium hypobromite or a mixture of potassium iodate, iodide and sulfuric acid. The resulting derivatives are sometimes contaminated with trihalogenated anilines formed during the reaction, but separation may be effected by means of sodium carbonate, in which the impurity is insoluble.

Compounds of the same type may also be obtained by the direct arsenation of halogenated anilines according to the Béchamp reaction; from halogenated nitro arsonic acids by treatment with reduced nickel under pressure; or by hydrolyzing the corresponding N-acylamino arsonic acids. The latter may be prepared by treating halogenated monoacyldiamino derivatives according to Bart's method, or by oxidizing the arsine-oxides with either mercuric oxide or hydrogen peroxide in alkaline solution.

The halogenated amino acids are lustrous, well-defined crystalline solids readily soluble in alkalis, insoluble in aqueous mineral acids, and are less basic than the amino arsonic acids. The acids containing one halogen atom can be more readily diazotized than those with two such substituents. The resulting diazo solutions are very stable—they can be warmed without evolution of nitrogen or conversion into phenolic compounds, while their ability to couple with various azo components remains unaffected. In addition they form triazo compounds with sodium azide. An interesting method of distinction between mono- and di-halogenated p-arsanilic acids is afforded by β-naphthoquinonesulfonic acid which forms a red condensation product with the first, but does not react with the second.

5-Chloro-2-aminophenylarsonic acid, $(Cl)(H_2N)C_6H_3AsO(OH)_2$, is prepared from arsenic acid and 4-chloroaniline by the Béchamp reaction; and consists of needles which melt at 207°, are sparingly soluble in cold water, ether or benzene but readily so in boiling water, methyl or ethyl alcohol.[948]

6-Chloro-3-aminophenylarsonic acid is produced upon reducing the corresponding nitro derivative in alkaline solution by means of hydrogen under pressure in the presence of reduced nickel. The product crystallizes in fine, white needles difficultly soluble in water, more easily in alcohol, and decomposing without melting when heated.[901]

3-Chloro-4-aminophenylarsonic acid may be obtained from 2-chloroaniline by the Béchamp reaction,[946] or by chlorinating acetyl-p-arsanilic acid with either chlorine in glacial acetic acid medium or with sodium hypochlorite in the presence of water, and subsequently removing the acetyl group by boiling with aqueous caustic soda.[1113] It consists of white needles, m. p. 305°; readily soluble in alkalis, methyl or ethyl

alcohol, sparingly so in hot water, dilute mineral acids or glacial acetic acid and insoluble in ether or acetone. When boiled with water, sodium acetate and sodium-β-naphthoquinonesulfonate, it yields a red solution, from which glacial acetic acid precipitates a red condensation product on standing.

3-Bromo-4-aminophenylarsonic acid results on brominating p-arsanilic acid in glacial acetic acid with half the theoretical amount of bromine:

$$2H_2N.C_6H_4AsO_3H_2 + Br_2 \longrightarrow$$
$$(Br)(H_2N)C_6H_3AsO_3H_2 + (HBr.H_2N)C_6H_4AsO_3H_2.$$

It forms white needles not melting below 255°; possesses the same solubilities as the corresponding chloro- compound, and reacts similarly with sodium-β-naphthoquinonesulfonate.[1114]

3-Iodo-4-aminophenylarsonic acid separates on treating p-arsanilic acid in methyl alcohol with iodine in the presence of mercuric oxide. It consists of almost colorless needles readily soluble in methyl alcohol or alkalis, less so in ethyl alcohol, sparingly in glacial acetic acid or hot water and insoluble in acetone. It decomposes above 255°, and reacts with sodium-β-naphthoquinonesulfonate like the preceding compounds.[1115] On adding sodium azide to its diazo solution, it yields a white precipitate of 3-iodo-4-triazophenylarsonic acid, $H_2O_3AsC_6H_3\begin{matrix}\diagup I\\ \diagdown N_3\end{matrix}$, which is readily soluble in alkalis, methyl or ethyl alcohol but only sparingly so in cold water.[1016]

2,6-Dichloro-4-aminophenylarsonic acid, $(H_2N)Cl_2C_6H_2AsO_3H_2$, m. p. 197°, is made by hydrolyzing the corresponding acetyl derivative with dilute alkali.[616]

3,5-Dichloro-4-aminophenylarsonic acid, formed on chlorinating p-arsanilic acid in glacial acetic acid, crystallizes in lustrous needles which do not melt below 255°, are readily soluble in methyl alcohol or alkalis, less so in ethyl alcohol or glacial acetic acid, sparingly in hot water and insoluble in acetone. It does not react with sodium-β-naphthoquinonesulfonate.[1116] It yields a white, crystalline triazo compound upon diazotizing and treating with sodium azide.[648]

3,5-Dibromo-4-aminophenylarsonic acid exists as almost colorless needles resembling the corresponding dichloro derivative in its properties. It is obtained by the action of sodium hypobromite upon p-arsanilic acid dissolved in cold dilute hydrochloric acid.[1116]

3,5-Diiodo-4-aminophenylarsonic acid results upon adding aqueous potassium iodide to a similar solution of p-arsanilic acid, dilute sulfuric acid and potassium iodate and warming on a water-bath. The product crystallizes in almost colorless needles readily soluble in alkalis or methyl alcohol, less so in ethyl alcohol or acetic acid, difficultly soluble in hot water and insoluble in ether or acetone. It does not melt below 250°.[1117]

3-Chloro-4-acetylaminophenylarsonic acid,

$$(CH_3CO.HN)ClC_6H_3AsO(OH)_2,$$

is obtained by the action of either chlorine or sodium hypochlorite upon acetyl-p-arsanilic acid suspended in glacial acetic acid.[1118]

2-Chloro-4-allylthiocarbamidophenylarsonic acid,

$$(C_3H_5NHCSHN)(Cl)C_6H_3AsO(OH)_2,$$

prepared from 2-chloro-p-arsanilic acid and allyl mustard oil decomposes without melting when heated.[963]

2,6-Dichloro-4-acetylaminophenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{cases} Cl \\ Cl \\ NHOCCH_3 \end{cases},$$

is made from 1-amino-2,6-dichloro-4-acetylaminobenzene by Bart's method. It is insoluble in cold water, readily soluble in hot water, alcohol or alkalis, and does not melt at 250°.[616]

2-Chloro-4-methylaminophenylarsonic acid,

$$(H_3C.HN)(Cl)C_6H_3AsO_3H_2,$$

is prepared by oxidizing the corresponding arsineoxide with hydrogen peroxide in alkaline solution. It is a white powder melting at 211°, insoluble in cold water, acetone or chloroform but soluble in hot water or alcohol.[532]

2-Chloro-4-dimethylaminophenylarsonic acid,

$$[(CH_3)_2N](Cl)C_6H_3AsO_3H_2,$$

is produced like the preceding acid, and consists of a white powder melting above 300°, insoluble in cold water or alcohol, slightly soluble in hot alcohol, cold concentrated hydrochloric acid or glacial acetic acid and easily soluble in aqueous alkalis.[533]

2-Bromo-4-dimethylaminophenylarsonic acid decomposes at 235°. It is derived from the corresponding arsineoxide by oxidation with either mercuric oxide or hydrogen peroxide in alkaline solution.[1119]

2,6-Dichloro-4-dimethylaminophenylarsonic acid,

$$H_2O_3AsC_6H_2\left\langle\begin{array}{l}Cl\\ Cl\\ N(CH_3)_2\end{array}\right. ,$$

from 2,6-dichloro-4-aminophenylarsonic acid by treatment with dimethyl sulfate, is a reddish powder insoluble in dilute acids, cold water, benzene or acetone but soluble in alkalis, hot alcohol or glacial acetic acid.[616]

13. *Nitro Amino Aryl Arsonic Acids.*—Since direct nitration of unsubstituted amino arylarsonic acids yields a mixture of various products, such as the mono- and dinitro derivatives, diazo arsonic acids, etc., various indirect methods have been devised for the introduction of nitro groups into the nuclei of amino arsonic acids, the most satisfactory of which depend upon:

1. The nitration of carbethoxy-, acetyl- or oxalylamino arsonic acids and subsequent removal of the acyl group by hydrolysis.

2. Replacement of the free amino group of a nitroacetyldiamine by an arsonic acid radical according to Bart's method, and splitting off the acetyl group.

In one case the desired result has been obtained by replacing the halogen atom of a halogenated nitroarsonic acid with an amino group by heating with ammonia in an autoclave. In addition to these indirect methods, it has been found possible to arsenate both ortho and para nitroanilines directly by Béchamp's reaction.

The products are yellowish crystalline solids which are soluble in alkalis or hot water, less so in mineral acids, and can be readily reduced to the corresponding diamino acids. The most interesting member of this chapter is 3-nitro-4-aminophenylarsonic acid. When warmed with concentrated alkali solution, its amino group is split off as ammonia and replaced by a hydroxyl:

$$C_6H_3\left\langle\begin{array}{l}AsO_3H_2\\ NO_2\\ NH_2\end{array}\right. \longrightarrow C_6H_3\left\langle\begin{array}{l}AsO_3H_2\\ NO_2\\ OH\end{array}\right. .$$

It can be readily diazotized and the resulting diazo compound converted into a triazo derivative by treating with sodium azide; into 3-nitro-

phenylarsonic acid with hypophosphorous acid; or into a hydroxy-diazo arsonic acid by treating with sodium acetate:

$$C_6H_3\begin{cases} AsO_3H_2 \\ NO_2 \\ N=NX \end{cases} \xrightarrow[\text{acetate}]{\text{Sodium}} C_6H_3\begin{cases} AsO_3H_2 \\ OH \\ N=NX \end{cases} .$$

On boiling the above nitro diazo arsonic acid in mineral acid solution, no replacement of the diazo group by a hydroxyl occurs, the arsenic being split off instead. The only dinitro amino acid thus far prepared is characterized by its inability to yield a diazo compound by any of the known methods.

The N- substituted nitro amino arsonic acids which behave like a nitro compound as well as a substituted amino acid, are prepared by nitrating the corresponding N- substituted amino arsonic acids; from N- monosubstituted diamines by Bart's method; or from halogenated nitro arsonic acids by condensing with various amino derivatives:

$$R\begin{cases} AsO_3H_2 \\ NO_2 \\ X \end{cases} + H_2N.R' \longrightarrow R\begin{cases} AsO_3H_2 \\ NO_2 \\ NH.R' \end{cases} + HX \quad (X = \text{halogen}).$$

5-Nitro-2-aminophenylarsonic acid, $H_2O_3AsC_6H_3(NO_2)NH_2$. — 4-Nitroaniline, unlike other p- substituted aromatic bases, gives good results when condensed with arsenic acid by the Béchamp reaction at 210°. The product consists of lustrous, orange-yellow prisms melting with decomposition at 235-6°, sparingly soluble in water or dilute acids in the cold, but readily on heating, and readily soluble in alkali hydroxides or carbonates, sodium acetate, methyl or ethyl alcohol. It can be diazotized in mineral acid solution, yielding a soluble, almost colorless diazonium compound which couples readily to form azo derivatives, and whose diazo group may be replaced by hydrogen, forming 3-nitrophenylarsonic acid. Boiling the nitro amino arsonic acid with potassium iodide and sulfuric acid converts it into o-iodo-p-nitroaniline; on reduction it yields p-phenylenediaminearsonic acid, while warming with caustic potash causes a replacement of the amino group by a hydroxyl.[1120]

2-Nitro-3-aminophenylarsonic acid is obtained by hydrolyzing the corresponding nitrocarbethoxyaminophenylarsonic acid with concentrated sulfuric acid at 70-80°, pouring on ice, and then neutralizing with caustic soda. It forms orange-yellow needles sparingly soluble in dilute mineral acids or hot water. It is converted into the corre-

sponding nitro hydroxy arsonic acid by boiling concentrated potassium hydroxide solution,[724] and into a granular, yellow triazo compound,

$$H_2O_3AsC_6H_3\begin{matrix} \diagup NO_2 \\ \\ \diagdown N_3 \end{matrix},$$

by diazotizing and treating with sodium azide.[1121]

6-Nitro-3-aminophenylarsonic acid.—m-Arsanilic acid is first converted into its oxalyl derivative, which is then dissolved in sulfuric acid, nitrated at 0-5°, and the resulting substance hydrolyzed by boiling with 2N-hydrochloric acid. The product separates as pale yellow needles, whose amino group may be replaced by a hydroxyl as above.[1122]

2-Nitro-4-aminophenylarsonic acid is prepared by treating 2-nitro-4-acetyl-p-phenylenediamine according to Bart's method and subsequently hydrolyzing to remove the acetyl group. It crystallizes in orange-yellow needles which darken at 240°, decompose at 258°, and are sparingly soluble in cold water, dilute mineral acids or alcohol, though more soluble in methyl alcohol, glacial acetic acid, alkalis or sodium acetate.[1123]

3-Nitro-4-aminophenylarsonic acid may be prepared either by nitrating 4-oxalylaminophenylarsonic acid and subsequently hydrolyzing;[1105] by heating 4-chloro-3-nitrophenylarsonic acid with ammonia in an autoclave at 120° and acidifying with hydrochloric acid;[928] by nitrating carbethoxy-p-arsanilic acid at 0-5° and hydrolyzing;[1019] or by the direct arsenation of o-nitroaniline at 200-10.[85] It forms yellow needles readily soluble in hot water, 50% acetic acid, cold methyl or ethyl alcohol, alkalis or concentrated mineral acids, sparingly in glacial acetic acid and insoluble in dilute acids, acetone or ether. With hydriodic acid it yields successively 3-nitro-4-aminophenyldiiodoarsine and 4-iodo-2-nitroaniline. On heating with alkali the amino group is replaced by a hydroxyl [distinction from these isomers in which the nitro and amino groups are in meta or para position to each other].[1124, 1125] It can be readily diazotized to 3-nitro-4-diazophenylarsonic acid which when coupled with R-salt in alkaline solution yields a red solution, while with resorcin an orange-yellow solution results. By treating this diazo-compound with sodium acetate, the nitro group is replaced by a hydroxyl;[1126] reduction with hypophosphorous acid produces 3-nitrophenylarsonic acid, while boiling in mineral acid solution splits off the arsenic. With sodium azide, the above diazo compound yields the corresponding triazo compound. The latter separates from dilute alcohol

as a yellow, crystalline powder which loses nitrogen 73-5°, forming 3,4-dinitrosophenylarsonic acid.[1121]

The sodium, ammonium, silver, barium, calcium and copper salts, as well as the methyl and ethyl esters of the above arsonic acid have been prepared.

5-Nitro-4-amino-3-methylphenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{cases} NO_2 \\ NH_2 \\ CH_3 \end{cases},$$

results on nitrating either 4-acetylamino-3-methylphenylarsonic acid,[1127] or 4-oxalylamino-3-methylphenylarsonic acid,[961] and removing the acyl group by hydrolysis. It exists as orange needles containing $1\frac{1}{2}$ molecules of water of crystallization, and is readily soluble in hot water. The amino group is replaced by a hydroxyl on heating the acid with concentrated caustic potash solution.

3,5-Dinitro-4-aminophenylarsonic acid, $H_2O_3AsC_6H_2(NO_2)_2(NH_2)$, is produced by nitrating 3-nitro-p-arsanilic acid at 0-5°,[928] or by similarly treating p-arsanilic acid in concentrated sulfuric acid solution at 5° or below, allowing to stand for two hours at 10-15° and then pouring upon ice.[1128] The admixture of trinitroaniline formed in the latter method is removed by dissolving the precipitate in aqueous soda, and extracting with ether. The acid separates as brownish-yellow, lustrous needles or leaflets, readily soluble in alkali hydroxides or carbonates and in sodium acetate, sparingly in water, alcohol or dilute mineral acids. It does not give the characteristic red coloration of dinitroanilines with alcoholic potash, and cannot be diazotized. On treating its alkaline solution with bromine, 4-bromo-2,6-dinitroaniline is obtained, while on warming with dilute caustic potash, ammonia is liberated and the amino group replaced by a hydroxyl. With concentrated caustic potash, however, it yields a violet coloration changing to brownish red.

2-Nitro-3-carbethoxyaminophenylarsonic acid,

$$H_2O_3AsC_6H_3(NO_2)(NH.COOC_2H_5),$$

obtained by nitrating the corresponding carbethoxy arsonic acid at 0-5°, is a pale yellow, crystalline powder sparingly soluble in water but readily in alkalis.[724]

3-Nitro-4-carbethoxyaminophenylarsonic acid, similarly prepared, crystallizes in yellowish needles slightly soluble in water.[1013]

5-Nitro-2-acetylaminophenylarsonic acid,

$$(CH_3CO.HN)(O_2N)C_6H_3AsO_3H_2,$$

is made by acetylating the corresponding amino arsonic acid.[1120]

2-Nitro-4-acetylaminophenylarsonic acid is formed as an intermediate product in the preparation of 2-nitro-4-aminophenylarsonic acid from 2-nitro-4-acetyl-p-phenylenediamine by Bart's method. It consists of yellowish-white, microcrystalline needles readily soluble in hot water, alcohol, glacial acetic acid or alkalis but sparingly in dilute mineral acids. On heating with dilute sulfuric acid the acetyl group is removed.[1123]

2-Nitrophenylglycine-4-arsonic acid,

$$H_2O_3AsC_6H_3(NO_2)(NH.CH_2COOH),$$

results upon refluxing a solution of 4-chloro-3-nitrophenylarsonic acid in 5N-caustic soda with aminoacetic acid for 30 hours at 50°, and then acidifying. The yellow-colored product is insoluble in acetone, ether or glacial acetic acid, dissolves in hot alcohol, cold alkali or hot water, and decomposes with faint intumescence when heated.[928]

3-Nitro-4-benzenesulfamidophenylarsonic acid,

$$H_2O_3AsC_6H_3(NO_2)(NH.SO_2C_6H_5).$$

4-Chloro-3-nitrophenylarsonic acid and benzensulfonamide dissolved in 5N-sodium hydroxide are heated in an autoclave at 120° for two hours, then 150° for 9 hours and finally precipitated with dilute acid. On removing the admixture of unchanged benzenesulfonamide with ether the product remains as a pale brown substance easily soluble in alkali, hot water or alcohol, less so in acetone and insoluble in ether.[928]

5-Nitro-2-aminophenylarsonic oxanilide,

$$\begin{array}{l} CO.HN(NO_2)C_6H_3AsO(OH)_2 \\ | \\ CO.HN(NO_2)C_6H_3AsO(OH)_2 \end{array},$$

may be prepared by grinding together 5-nitro-2-aminophenylarsonic acid, oxalic acid and 10N-sodium hydroxide, heating the mass in an oil bath at 110-130° until all the water has been driven off, and finally heating the resulting solid at 160-5°.[1112]

2,6-Dinitrophenylglycine-4-arsonic acid,

$$H_2O_3AsC_6H_2(NO_2)_2(NH.CH_2COOH),$$

obtained from 4-chloro-3,5-dinitrophenylarsonic acid and aminoacetic acid dissolved in N-caustic soda, is a yellowish-green powder intumescing

on heating; dissolves in alkalis, hot water, alcohol, glacial acetic acid or acetone, but is insoluble in ether.[928]

3,5-Dinitro-4-benzenesulfamidophenylarsonic acid,

$$H_2O_3AsC_6H_2(NO_2)_2(NH.SO_2C_6H_5),$$

is made from 4-chloro-3,5-dinitrophenylarsonic acid and benzenesulfonamide by the method employed in the preparation of the corresponding mononitro compound. It is a brownish substance which decomposes with intumescence on heating; is soluble in alkalis, hot water, alcohol or glacial acetic acid and insoluble in ether, cold glacial acetic acid or dilute acids.[928]

3-Nitro-4-methylaminophenylarsonic acid,

$$H_2O_3AsC_6H_3(NO_2)(NH.CH_3),$$

results on heating the sodium salt of 3-nitro-4-chlorophenylarsonic acid with methylamine hydrochloride in an autoclave at 100°. It is a yellow substance which intumesces on heating, is easily soluble in alkalis, sodium acetate or hot alcohol, difficultly so in cold alcohol, practically insoluble in water or dilute mineral acids and insoluble in acetone or ether.[928]

2-Chloro-5-nitro-4-methylaminophenylarsonic acid,

$$H_2O_3AsC_6H_2(NO_2)(Cl)(NH.CH_3),$$

consists of yellow needles produced by warming 2,4-dichloro-5-nitrophenylarsonic acid with an aqueous solution of methylamine.[909]

3,5-Dinitro-4-methylaminophenylarsonic acid,

$$H_2O_3AsC_6H_2(NO_2)_2(NH.CH_3),$$

is a lemon-yellow crystalline powder obtained by nitrating 3-nitro-4-methylaminophenylarsonic acid;[909] by warming alcoholic 4-chloro-3,5-dinitrophenylarsonic acid with methylamine in the same solvent;[928] or by treating a sulfuric acid solution of 3,5-dinitro-4-methylnitraminophenylarsonic acid with mercury and shaking for some time, then pouring on ice, separating from metallic mercury, and finally decomposing the yellow precipitate with either sodium hydroxide or carbonate.[606] The compound melts with decomposition at about 164°; dissolves in alkalis, hot water, alcohol, glacial acetic acid or aqueous sodium acetate, but is insoluble in mineral acids, acetone or ether.

2-Chloro-3,5-dinitro-4-methylaminophenylarsonic acid,

$$H_2O_3AsC_6HCl(NO_2)_2(NH.CH_3),$$

is prepared by nitrating the corresponding 5-nitro compound at 0°. It crystallizes from water in which it is difficultly soluble, and melts with decomposition at 196°.[909]

3,5-Dinitro-4-methylnitraminophenylarsonic acid,

$$H_2O_3AsC_6H_2(NO_2)_2N\left\langle\begin{array}{l}CH_3\\ NO_2\end{array}\right. ,$$

is derived from aromatic arsenicals in which the p-position to the arsenic is occupied by the group $—N\left\langle\begin{array}{l}CH_3\\ R\end{array}\right.$ (where R stands for hydrogen as in N-methylaminophenylarsonic acid, or for an acid residue as in either N-acetylmethylaminophenylarsonic acid or N-nitrosomethylaminophenylarsonic acid), by nitrating with a mixture of fuming nitric and concentrated sulfuric acids.[1091] It may also be obtained by similarly nitrating 3-nitro-4-methylaminophenylarsonic acid,[928] 4-dimethylaminophenyldichloroarsine, the corresponding arsineoxide or arsonic acid.[1129, 1130]

In all cases the nitration-product is warmed on the water-bath for several hours prior to its precipitation upon ice. The product is readily soluble in hot alcohol or acetone, in glacial acetic acid, sodium acetate solution, alkali hydroxides or carbonates, but is insoluble in dilute mineral acids. When heated on a platinum foil it deflagrates.

2-Chloro-3,5-dinitro-4-methylnitraminophenylarsonic acid,

$$H_2O_3AsC_6HCl(NO_2)_2N\left\langle\begin{array}{l}CH_3\\ NO_2\end{array}\right. ,$$

is formed on nitrating 2-chloro-4-dimethylaminophenylarsineoxide at 5° like the preceding compound. It consists of a slightly yellowish powder soluble in aqueous sodium hydroxide, acetone, hot water, methyl or ethyl alcohol and insoluble in ether, chloroform or benzene. It explodes on heating.[618]

2-Bromo-3,5-dinitro-4-methylnitraminophenylarsonic acid is a yellow powder resembling the preceding acid both in method of preparation and properties.[618]

3,5-Dinitro-2-methylamino-4-methylnitraminophenylarsonic acid,

$$H_2O_3AsC_6H(NO_2)_2(NH.CH_3)N\left\langle\begin{array}{l}CH_3\\ NO_2\end{array}\right. ,$$

is a yellow powder soluble in alcohol, acetone or glacial acetic acid, insoluble in ether, chloroform or benzene, and exploding when heated. It results upon treating 2-chloro-3,5-dinitro-4-methylnitraminophenylarsonic acid with a solution of methylamine.[616]

N-(3-Nitrophenyl-4-arsonic acid)methylglycine amyl ester,

$$\begin{array}{l} H_3C \diagdown \\ \qquad N.C_6H_3(NO_2)AsO_3H_2, \\ H_{11}C_5OOC.CH_2 \diagup \end{array}$$

is prepared by treating 50 g. of N-(phenyl-4-arsonic acid)methylglycine amyl ester dissolved in 350 g. of sulfuric acid (228 c.c. conc. H_2SO_4 and 152 g. H_2O) with a mixture of one molecular proportion of nitric acid and 30 g. of 3:2 sulfuric acid at 38-40°. The product is precipitated in water as a dark yellow substance, m. p. 130°, slightly soluble in hot water but easily in alcohol. The amyl group may be removed by hydrolysis, yielding the free acid which is quite soluble in water.[1131]

N-(2-Nitrophenyl-4-arsonic acid)methylglycine amyl ester is made like its isomer except that the sulfuric acid used in the nitrating mixture is more dilute (1:3) and the reaction-temperature lower (10-20°). The free acid is obtained in the same way.[1131]

The ortho and meta nitro isomers of the *corresponding ethyl-* and *amylglycines* have also been prepared.[1131]

2-Nitro-4-dimethylaminophenylarsonic acid,

$$H_2O_3AsC_6H_3(NO_2)N(CH_3)_2,$$

results on nitrating the corresponding arsonic acid in concentrated sulfuric acid at 0°, and consists of golden yellow, long, flat needles sparingly soluble in hot water or alcohol, and melting at 204°.[1132]

3-Nitro-4-dimethylaminophenylarsonic acid may be produced either by nitrating a suspension of 4-dimethylaminophenylarsonic acid in glacial acetic acid and subsequently adding acetic anhydride,[1133] or by warming together on a water-bath alcoholic solutions of 4-chloro-3-nitrophenylarsonic acid and dimethylamine.[923] It crystallizes in small, yellow needles soluble in water, acids or hot alcohol, insoluble in ether or acetone, and intumescing on heating.

?-Nitro-4-dimethylamino-2-methylphenylarsonic acid,

$$H_2O_3AsC_6H_2 \begin{array}{l} \diagup NO_2 \\ -CH_3 \\ \diagdown N(CH_3)_2 \end{array},$$

is deposited on heating the corresponding dimethylamino arsonic aci with nitric acid (d, 1.2) in a sealed tube at 180°. The compound in tumesces upon heating.[1134]

?-*Nitro-4-dimethylamino-3-methylphenylarsonic acid,* similarly pre pared at 150°, decomposes at 208°.[1135]

3,5-Dinitro-4-dimethylaminophenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{cases}(NO_2)_2\\ N(CH_3)_2\end{cases},$$

may be obtained by digesting 3,5-dinitro-4-methoxyphenylarsonic aci with a 30% dimethylamine solution on a boiling water-bath;[608] or b nitrating the corresponding dimethylaminoarsonic acid with 30% nitri acid either at 40° for two hours, or at ordinary temperature for thre days.[1132] It separates in the form of yellow crystals melting wit decomposition at 161°, almost insoluble in cold water, slightly mor soluble in alcohol or acetone, but very easily soluble in the abov solvents when hot.

The mother liquor of the second process yields another dinitro com pound whose exact character has not yet been established. It con sists of small red plates which are less soluble in hot water than th yellow variety, and melt with decomposition at 158°.

3,5-Dinitro-4-diethylaminophenylarsonic acid,

$$H_2O_3AsC_6H_2(NO_2)_2[N(C_2H_5)_2],$$

is prepared like the preceding homologue, employing diethylamine. I is a yellow, crystalline substance easily soluble in alkalis, quite difficult so in cold but easier in hot water.[608]

3,5-Dinitro-4-piperidophenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{cases}(NO_2)_2\\ N(CH_2)_5\end{cases},$$

formed upon heating 3,5-dinitro-4-methoxyphenylarsonic acid with 50% piperidine solution, is a yellow, crystalline substance moderatel soluble in water.[608]

2,6-Dichloro-3,5-dinitro-4-methylnitraminophenylarsonic acid,

$$H_2O_3AsC_6Cl_2[NO_2]_2[N(CH_3)(NO_2)],$$

results upon nitrating 2,6-dichloro-4-dimethylaminophenylarsonic acid. It consists of a reddish powder decomposing at 200°, readily soluble in hot alcohol, aqueous sodium acetate or alkalis and insoluble in dilute acids, cold water or benzene.[616]

14. *Hydroxy Aryl Arsonic Acids.*—Phenols, like amines, may be arsenated directly by the Béchamp reaction, the arsonic acid radical entering the para position to the hydroxyl. The acids of this group may also be obtained either from amino arsonic acids by diazotizing and replacing the diazo group with a hydroxyl in the usual manner, or by treating amino phenols according to Bart's method or Mouneyrat's modification of the same. The dihydroxy arsonic acids may also be prepared by the above methods, with the exception of 3,4-dihydroxyphenylarsonic acid, which has been derived from the 4-hydroxy acid by treatment with potassium persulfate in alkaline solution.

The acids are crystalline solids generally soluble in water, alkalis, methyl or ethyl alcohol, or hot glacial acetic acid, either sparingly so or entirely insoluble in the other organic solvents, and form water-soluble alkali salts. With nascent halogens they yield the corresponding dihalogenated hydroxy arsonic acids together with more or less of the trihalogenated phenols. Some of the compounds, like the 2 and 3-hydroxy arsonic acids, couple readily with diazotized sulfanilic acid in alkaline solution, but the 4-isomer under these conditions gives up its arsenic in exchange for an azo group.

The hydrogen of the hydroxyl may in many instances be replaced by various acyl or alkyl radicals in the usual manner, yielding O-substituted hydroxy arsonic acids. The same products may also be obtained by oxidizing either the corresponding dichloroarsines with chlorine in aqueous medium, or the arsineoxides with hydrogen peroxide in alkaline solution; by the direct arsenation of alkoxy compounds, or from the corresponding amines by Bart's method.

2-Hydroxyphenylarsonic acid, $H_2O_3AsC_6H_4.OH$, is prepared by diazotizing a hydrochloric acid solution of o-arsanilic acid and warming until all the nitrogen is driven off.[1136] It is also obtained as a by-product in the direct arsenation of phenol,[1137] and in the preparation of o-phenylenediarsonic acid.[897] It crystallizes in long needles, m. p. 196° (J.), 190° (K.); readily soluble in methyl or ethyl alcohol, hot water or glacial acetic acid and sparingly in cold water, hot acetone or chloroform. It is distinguished from the meta and para isomers by the characteristic wine-red color it gives with ferric chloride solution. In alkaline solution it couples readily with diazotized sulfanilic acid, yielding a bright orange solution. It is readily precipitated from concentrated solutions of its salts by hydrochloric acid, redissolving in excess. Acetic acid does not readily liberate it from its salts.

The monosodium salt crystallizes with four molecules of water as

hexagonal platelets soluble in water. Its aqueous solution gives no immediate precipitate with calcium or barium ions, the latter coming down as a basic salt only after rendering the solution alkaline to phenolphthalein. Heavy metal ions produce immediate precipitates.

3-Hydroxyphenylarsonic acid is made by diazotizing m-arsanilic acid in sulfuric acid, expelling the nitrogen and isolating the compound through the lead salt. It crystallizes as rhombic crystals, m. p. 159-73°; readily soluble in water, methyl or ethyl alcohol, or in boiling acetic acid, sparingly so in hot acetone but insoluble in chloroform or benzene. In alkaline solution it couples readily with diazotized sulfanilic acid, producing a bright orange color.

The monosodium salt crystallizes in rosets of flat needles very soluble in water. Its aqueous solution yields precipitates with the salts of heavy metals but not with those of calcium or barium.[1138]

4-Hydroxyphenylarsonic acid (*Phenol-p-arsonic acid*) may be obtained in a number of ways. A stirred mixture of phenol (94 parts) and crystallized arsenic acid (151 parts) are heated for four hours at 150°, the resulting mass taken up with water, filtered and the filtrate evaporated to dryness in vacuo. From this solid the acid is extracted with acetone and finally recrystallized from glacial acetic acid.[1139] A modification of this method consists in heating the mixture of the constituents at 155-60° for seven hours, removing the unchanged arsenic acid by means of barium hydroxide, and isolating the acid either as such or as the sodium salt.[1140] The yield may be increased by working up the mother liquors.[1141]

By an easier method p-arsanilic acid (217 g.) is dissolved in water (2500 c.c.) and concentrated sulfuric acid (81.6 c.c.), diazotized with an aqueous solution of sodium nitrite (70 g. in 350 c.c.) at 0°, and the filtered solution warmed at 70° until all the nitrogen has been expelled. The excess of sulfuric acid is then removed by boiling with barium carbonate, the filtered solution treated with anhydrous sodium sulfate, decolorized with animal charcoal, and concentrated until the sodium salt crystallizes on cooling.[1142] This method has also been modified by diazotizing atoxyl in hydrochloric acid, evaporating the diazo solution to dryness, and extracting the dried residue with hot acetone, from which the free acid crystallizes.[1143]

Finally, the arsonic acid may be prepared from p-aminophenol either by Bart's original method,[86, 1144] or by Mouneyrat's modification.[89]

The free acid crystallizes in almost colorless prisms, m. p. 173-4°; readily soluble in cold water, alcohol or dilute mineral acids, less so in cold acetone and very sparingly in ether or ethyl acetate. It is decomposed by bromine water, yielding tribromophenol, while on attempting to couple it with diazo compounds the arsenic is split off and replaced by the azo group, thereby resembling p-hydroxybenzoic acid. On the other

hand, it condenses readily with tetramethyldiaminobenzhydrol to the leuco compound, $(H_2O_3As)(HO)C_6H_3.CH\begin{matrix} \diagup C_6H_4.N(CH_3)_2 \\ \diagdown C_6H_4.N(CH_3)_2 \end{matrix}$, which can be oxidized to the corresponding dye.[1145]

The sodium salt, $HO.C_6H_4AsO_3HNa$, when treated successively with molybdenum trioxide and guanidinium chloride in aqueous solution, yields a mixture of white needles and plates,[1146] the first corresponding to the formula $(CN_3H_6)_2\left[As\begin{matrix} C_6H_4.OH \\ (MoO_4)_3 \end{matrix}\right].2H_2O$.

4-Hydroxy-2-methylphenylarsonic acid (*m-Cresol-p-arsonic acid*), $H_2O_3AsC_6H_3\begin{matrix} \diagup OH \\ \diagdown CH_3 \end{matrix}$, results from the direct arsenation of m-cresol at 170°. It sinters at 160°; melts with decomposition at 183-5°, and resembles the succeeding isomeride in its physical and chemical properties.[1139]

4-Hydroxy-3-methylphenylarsonic acid (*o-Cresol-p-arsonic acid*) may be obtained from o-cresol and arsenic acid by heating together at 140°, extracting the cooled mass with aqueous sodium carbonate, and removing the excess o-cresol with ether. The solution is then acidified, evaporated to dryness in vacuo, and the arsonic acid extracted therefrom by means of acetone.[1139] The compound may also be produced from 4-amino-3-methylphenylarsonic acid by diazotizing in sulfuric acid solution and replacing the diazo group with a hydroxyl by means of steam.[1147] The compound forms yellowish crystals sintering at 150°, and melting with decomposition at 172°. It crystallizes from water as white prisms containing $1H_2O$ and melting at 180°, but when dehydrated it melts at 222° (Benda). It is readily soluble in hot water, methyl or ethyl alcohol, acetone, glacial acetic acid, alkali hydroxides or carbonates and in mineral acids, but sparingly in carbon bisulfide, benzene, ethyl acetate, ether, chloroform or ligroin.

The monosodium salt crystallizes from water with $2H_2O$ in the form of plates soluble in cold water with a neutral reaction but only sparingly soluble in alcohol.[1143]

4-Hydroxy-α-naphthylarsonic acid (*α-Naphthol-4-arsonic acid*),

$$H_2O_3AsC_{10}H_6.OH,$$

made by decomposing the diazo derivative of α-naphthylaminearsonic acid with steam, is isolated through the sodium salt, which consists of

well-defined needles. The free acid forms colorless needles or platelets readily soluble in hot water or alcohol and practically insoluble in ether, chloroform or petroleum ether. Its alkali salts are readily soluble in water, but those of the heavy metals are practically insoluble.[949]

4-Hydroxyanthraquinone-1-arsonic acid,

$$\begin{array}{ccc} & \mathrm{CO} & \\ & \diagup \qquad \diagdown & \\ (\mathrm{H_2O_3As})(\mathrm{OH})\mathrm{C_6H_2} & & \mathrm{C_6H_4}. \\ & \diagdown \qquad \diagup & \\ & \mathrm{CO} & \end{array}$$

1,4-Aminohydroxyanthraquinone is dissolved in concentrated sulfuric acid, diazotized with "nitrose" (containing about 47 per cent of nitrosylsulfuric acid) and coupled with sodium arsenite. It is then warmed to about 60°, left over night, filtered, and solid sodium chloride added to precipitate the sodium salt, from which the free acid is obtained by treating its aqueous solution with hydrochloric acid. The compound consists of yellow, felted needles decomposing indefinitely above 200°, somewhat soluble in water, boiling methyl or ethyl alcohol, easily soluble in concentrated sulfuric acid, aqueous soda or alkali, hot sodium acetate or boiling glacial acetic acid. When dissolved in two molecular proportions of alkali and precipitated with alcohol, red flakes are obtained, but when three molecules of alkali are used the result is a brown-violet salt which is dissociated in water. Magnesia mixture produces a brown-red precipitate even in the cold.[1148]

2,4-Dihydroxyphenylarsonic acid (Resorcinolarsonic acid),

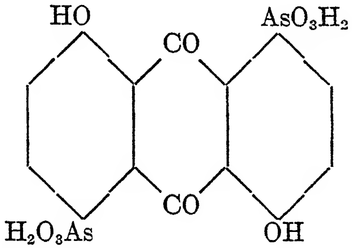
$$H_2O_3AsC_6H_3(OH)_2,$$

is made from resorcinol and 83 per cent arsenic acid solution by heating on a water bath for two days. It forms colorless prisms, m. p. 191°; readily soluble in water, methyl or ethyl alcohol, sparingly so in glacial acetic acid or acetone and insoluble in ether, benzene or petroleum ether. With ferric chloride solution it gives a deep red coloration, but it does not reduce ammoniacal silver nitrate even upon warming.[1149]

3,4-Dihydroxyphenylarsonic acid is prepared by treating an aqueous solution of 4-hydroxyphenylarsonic acid successively with 10N-caustic soda and powdered potassium persulfate. After 48 hours' stirring the liquid is mixed with hydrochloric acid, boiled for 15 minutes and treated with ammonia and an excess of magnesia mixture. On boiling there separates the magnesium salt, from which the free acid is obtained by treating with hydrochloric acid. The compound is extremely soluble in water and differs from 4-hydroxyphenylarsonic acid in its powerful reducing action on ammoniacal silver nitrate in the cold, and by giving

with acid ferric chloride the green coloration characteristic of catechol derivatives.[1150]

4,8-Dihydroxyanthraquinone-1,5-diarsonic acid,



(*Anthrarufindiarsonic acid*), is formed from 1,5-diamino-4,8-dihydroxy-anthraquinone by Bart's reaction. It is a yellow to brownish-yellow microcrystalline compound soluble in 10N-hydrochloric or concentrated sulfuric acid, N-sodium hydroxide, 2N-soda and hot 2N-sodium acetate, soluble in traces in hot water and entirely insoluble in methyl or ethyl alcohol, glacial or 50 per cent acetic acid, or N-hydrochloric acid. The diarsonic acid does not have a sharp melting or decomposition point, but when heated it turns violet at about 270°. Its disodium salt is violet while the tetra(?)sodium salt is orange.[1151]

5,5'-Dihydroxy-2,2'-stilbenediarsonic acid,

$$H_2O_3As(OH)C_6H_3.CH = HC.C_6H_3(OH)AsO_3H_2,$$

is obtained from the corresponding diamino compound by diazotizing and replacing the diazo groups with hydroxyls in the usual manner.[621]

4-Acetoxyphenylarsonic acid, $(CH_3CO.O)C_6H_4AsO_3H_2$, is produced by acetylating the corresponding hydroxy acid with acetic anhydride in the presence of a small quantity of concentrated sulfuric acid. It crystallizes from acetone in clusters of fine needles which do not melt below 250°, are readily soluble in cold water but sparingly in cold alcohol or acetone.

The monosodium salt crystallizes from water with $3H_2O$ as clusters of fine silky needles readily soluble in water with a neutral reaction and sparingly in alcohol.[1143]

4-Acetoxy-3-methylphenylarsonic acid, $H_2O_3AsC_6H_3\begin{matrix} / CH_3 \\ \backslash O.COCH_3 \end{matrix}$, is obtained from the corresponding hydroxy acid as in the preceding

homologue, and separates in clusters of fine needles, m. p. 164-6°; sparingly soluble in cold water or acetone and readily in alcohol.

The monosodium salt crystallizes with four molecules of water in radial clusters of silky needles readily soluble in water with a neutral reaction and sparingly in alcohol.[1152]

(Phenyl-4-arsonic acid) hydroxyacetic acid [*Phenoxyacetic acid-p-arsonic acid; Phenylglycol-p-arsonic acid*], $H_2O_3AsC_6H_4(O.CH_2COOH)$.—From concentrated aqueous sodium 4-hydroxyphenylarsonate by refluxing for several hours with two moles of chloroacetic acid and 3.5 to 4 moles of caustic soda. It crystallizes from water or glacial acetic acid as spear-shaped crystals or platelets soluble in methyl or ethyl alcohol but almost insoluble in ether or benzene. It sinters above 150°, carbonizes at higher temperatures, and forms easily soluble salts with alkali hydroxides or carbonates.[1153]

(Phenyl-4-arsonic acid) hydroxyacetic methyl ester,

$$H_2O_3As.C_6H_4(O.CH_2COOCH_3),$$

formed when the preceding acid is refluxed for two hours with a mixture of dry methyl alcohol and a little concentrated sulfuric acid, crystallizes in lustrous plates which partially melt with gas evolution at about 192-5°, decompose at higher temperature, and dissolve readily in methyl alcohol, hot ethyl alcohol or water but sparingly in cold alcohol or water.[1154]

(Phenyl-4-arsonic acid) hydroxyacetamide,

$$H_2O_3AsC_6H_4(O.CH_2CONH_2),$$

is prepared by the action of ammonia on the preceding compound, and crystallizes as microscopic rhombic prisms, which do not melt below 280°, are sparingly soluble in cold water or hot alcohol but easily in boiling water. Its sodium salt separates slowly when the acid is dissolved in aqueous caustic soda, carefully neutralized with acetic acid, concentrated in vacuo to a small volume and finally treated with alcohol. It exists as glistening platelets easily soluble in water.[1154]

(Phenyl-4-arsonic acid) hydroxyacetanilide,

$$H_2O_3AsC_6H_4(OCH_2CONHC_6H_5),$$

results on boiling sodium 4-hydroxyphenylarsonate, chloroacetanilide and sodium iodide with a mixture of N-sodium hydroxide and alcohol for three hours. It forms glistening platelets sparingly soluble in cold, appreciably in hot water, alcohol or acetic acid and quite soluble in methyl alcohol. It does not melt below 280°.[1155]

(Phenyl-4-arsonic acid) hydroxyacetyl-3'-aminophenol,

$$H_2O_3AsC_6H_4(OCH_2CONHC_6H_4OH),$$

is produced by boiling sodium 4-hydroxyphenylarsonate together with m-chloroacetylaminophenol, and purifying through its sodium salt. The free acid is a heavy sandy, powder consisting of aggregates of irregular, microscopic leaflets which are slightly colored pink by impurities. They are sparingly soluble in boiling water or boiling acetic acid, more readily so in hot 50 per cent alcohol, and melt with decomposition at 238-40°.[1155]

(Phenyl-4-arsonic acid) hydroxyacetyl-4'-aminophenol is similarly obtained by employing p-chloroacetylaminophenol, and separates as colorless, microscopic crystals which upon heating gradually darken and decompose at 238-40°. It is very difficultly soluble in boiling water, methyl or ethyl alcohol but more easily in hot 50 per cent alcohol. On adding a few drops of sodium nitrite solution to a suspension of the acid in hot acetic acid, a clear, orange solution is obtained which deposits spherules of yellow crystals, probably a nitroso compound, on cooling.[1156]

(Phenyl-4-arsonic acid) hydroxyacetyl-4'-aminophenylurea,

$$H_2O_3AsC_6H_4(OCH_2CONHC_6H_4NHCONH_2),$$

consists of aggregates of microscopic needles prepared from sodium 4-hydroxyphenylarsonate and p-chloroacetylaminophenylurea by refluxing with a sodium iodide-alcohol mixture. It darkens and softens at about 230-40°, does not melt completely below 265°, and is practically insoluble in boiling water or 50 per cent alcohol.[1038]

(Phenyl-4-arsonic acid) thioacetic acid [Phenylthioglycol-p-arsonic acid], $H_2O_3AsC_6H_4(S.CH_2COOH)$.—p-Arsanilic acid is diazotized and coupled in soda solution with potassium xanthogenate, forming $C_2H_5OC.S.SC_6H_4AsO_3H_2$. This in turn is warmed with an alkaline solution of chloroacetic acid, concentrated and acidified. The product crystallizes from water as yellowish needles sintering at 170° and melting with decomposition at 187°. It is readily soluble in alkali hydroxides or carbonates, hot alcohol or glacial acetic acid but practically insoluble in ether or benzene.[1153]

2-Methoxyphenylarsonic acid, $CH_3O.C_6H_4AsO_3H_2$, results upon treating pure o-anisidine according to Bart's method, and crystallizes from alcohol as white needles, m. p. 193-4°.[151]

4-Methoxyphenylarsonic acid (p-Anisylarsonic acid) may be prepared by dissolving 4-methoxyphenylarsinetetrachloride in water;[489] by oxidizing a glacial acetic acid solution of 4-methoxyphenyldichloroarsine

with hydrogen peroxide;[493] by methylating an alkaline solution of sodium 4-hydroxyphenylarsonate with dimethyl sulfate;[1157] and finally by treating 4-methoxyaniline according to Mouneyrat's modification of Bart's method.[89] The product forms hard, colorless, crystalline crusts (M. & W.) or white compact crystals (M.) readily soluble in alcohol or hot water, sparingly in cold water, and melting at 159-60° (M. & W.), 203° (M.), 179-80° (B.). On heating the arsonic acid for several hours at 190-200° it loses one molecule of water forming an anhydride, $CH_3O.C_6H_4AsO_2$, the acid being regained by boiling the anhydride with water. When silver nitrate is added to a solution of the ammonium salt, a white precipitate of the disilver salt is obtained, while heating with aqueous phosphorous acid in a sealed tube at 100° produces 4,4′-dimethoxyarsenobenzene.

4-Methoxy-3-methylphenylarsonic acid, $H_2O_3AsC_6H_3\begin{matrix}\diagup CH_3\\ \diagdown OCH_3\end{matrix}$, results on methylating an alkaline solution of monosodium 4-hydroxy-3-methylphenylarsonate with dimethyl sulfate as in the preceding compound. It crystallizes from water in white, feathery needles which do not melt below 260°.[1158]

4-Ethoxyphenylarsonic acid, $C_2H_5O.C_6H_4AsO_3H_2$, is obtained by treating 4-ethoxyphenyldichloroarsine with chlorine in the presence of warm water;[622] from p-ethoxyaniline by Mouneyrat's modification of Bart's process;[89] and finally by diazotizing a dry alcohol-hydrochloric acid solution of p-arsanilic acid with ethylnitrite and warming until the evolution of nitrogen is complete.[1142] The product crystallizes from water as white prisms melting according to Michaelis at 209-10°, although Bertheim found that on rapid heating it melted at 185° with foaming, then resolidified and did not melt again below 245°. Its calcium, copper and silver salts are insoluble in water.

4-Methoxy-3-hydroxyphenylarsonic acid, $H_2O_3AsC_6H_3\begin{matrix}\diagup OH\\ \diagdown OCH_3\end{matrix}$, is produced from 5-nitroguaiacol by first reducing with tin and hydrochloric acid, diazotizing the resulting solution with sodium nitrite and then coupling with arsenious acid in alkaline solution. The product crystallizes from water with one molecule of the solvent as short, flattened prisms, m. p. 189°; sparingly soluble in alcohol or the other usual organic solvents. The ammoniacal solution yields a precipitate with calcium chloride, while warming with hypophosphorous acid reduces it to the corresponding arseno compound.[624]

2-Methoxy-4-hydroxyphenylarsonic acid is made by heating the monomethyl ether of resorcinol with arsenic acid on a water bath for 50 hours. It crystallizes as colorless crystals, m. p. 209°; readily soluble in water, glacial acetic acid, methyl or ethyl alcohol, sparingly in acetone and insoluble in ether.[1159]

3-Methoxy-4-hydroxyphenylarsonic acid is prepared from 4-nitroguaiacol like the 4-methoxy-3-hydroxy isomer, and crystallizes with one molecule of water as glistening, rhombic prisms which, after drying at 110°, melt at 190°. It is sparingly soluble in cold alcohol or water, but readily so in acetic acid or hot water. The ammoniacal solution of the acid yields a crystalline precipitate of the calcium salt with calcium chloride, while warming with dilute hypophosphorous acid yields the corresponding arseno compound.[626]

4-Acetoxy-3-methoxyphenylarsonic acid, $H_2O_3AsC_6H_3\begin{array}{l}\diagup OCH_3\\ \diagdown O.COCH_3\end{array}$, separates from ethyl acetate containing a little alcohol as colorless, glistening plates melting at 186°, easily soluble in water or alcohol but sparingly in ether or ethyl acetate.[626]

3-Acetoxy-4-methoxyphenylarsonic acid crystallizes from benzene containing a little alcohol in woolly needles gradually decomposing above 200°, readily soluble in water, alcohol or ethyl acetate but very sparingly so in benzene or light petroleum.[624]

Benzoylguaiacolarsonic acid, $H_2O_3AsC_6H_3\begin{array}{l}\diagup OCH_3\\ \diagdown O.OCC_6H_5\end{array}$, is obtained by oxidizing the corresponding arsineoxide with hydrogen peroxide. It crystallizes from acetone as odorless needles decomposing at higher temperatures without melting, insoluble in ether but soluble in acetone or soda solution.[499]

2,4-Dimethoxyphenylarsonic acid, $H_2O_3AsC_6H_3(OCH_3)_2$, is made either by heating resorcinoldimethyl ether with arsenic acid on a water bath for eight days,[1160] or by treating an alkaline solution of 2,4-dihydroxyphenylarsonic acid with dimethyl sulfate at 30-50°.[1161] The acid consists of lustrous needles, m. p. 242-3°; readily soluble in water, methyl or ethyl alcohol and in glacial acetic acid but very sparingly in ether.

3,4-Dimethoxyphenylarsonic acid is formed from aminoveratrole by Bart's method, and consists of colorless, rhombic prisms very sparingly

soluble in acetone but readily so in alcohol or hot water. When placed in a bath at 170° it finally melts at 192°, but when slowly heated it sinters and remains unmelted between 180 and 190° due to the readiness with which anhydride formation takes place. Its ammoniacal solution yields a precipitate of small needles on boiling with calcium chloride, and an amorphous precipitate with magnesia mixture. Warm dilute hypophosphorous acid reduces it to the corresponding arseno compound, while with hydrobromic acid at 100° or with hydrochloric acid at 130-60° partial decomposition results.[627]

15. *Halogenated Hydroxy Aryl Arsonic Acids.*—3-Chloro-4-hydroxyphenylarsonic acid, $H_2O_3AsC_6H_3{<}^{Cl}_{OH}$, is made by diazotizing 3-amino-4-hydroxyphenylarsonic acid, and boiling the diazo compound with a hydrochloric acid solution of cupric chloride until the evolution of nitrogen has ceased. The whole is then treated with hot alkali, acidified and concentrated.[1162]

3,5-Dichloro-4-hydroxyphenylarsonic acid, $H_2O_3AsC_6H_2{<}^{Cl_2}_{OH}$, is formed along with some trichlorophenol upon treating sodium 4-hydroxyphenylarsonate with sodium hypochlorite and subsequently acidifying with hydrochloric acid. The admixture of trichlorophenol is removed with ether. The above arsonic acid forms prisms which do not melt below 260°, are readily soluble in acetone, methyl or ethyl alcohol, sparingly in water and insoluble in ether or chloroform.[1163]

3,5-Dibromo-4-hydroxyphenylarsonic acid is similarly prepared employing sodium hypobromite.[1163]

3,5-Diiodo-4-hydroxyphenylarsonic acid may be obtained by allowing p-hydroxyphenylarsonic acid to react with potassium iodide, potassium iodate and sulfuric acid at water-bath temperature. It is a crystalline substance readily soluble in methyl alcohol but slightly so in ethyl alcohol, acetone or acetic acid. It does not melt below 260°, and decomposes at higher temperature with liberation of iodine.[1163]

16. *Nitro Hydroxyaryl Arsonic Acids.*—Unlike the aminoarsonic acids, the corresponding hydroxy acids may be readily nitrated in the usual manner, yielding mono- or dinitro hydroxy arsonic acids, depending upon the quantity of nitrating acid used and the temperature. The mononitro derivatives may also be prepared from nitroaminophenol

by Bart's method; from either nitroaminoarsonic acids containing the nitro and amino groups in ortho position to each other, or nitrodimethylamino acids by warming with concentrated caustic alkalis; or by hydrolyzing nitromethoxyarsonic acids with aqueous soda.

The products are yellowish crystalline solids soluble in alkalis, glacial acetic acid, acetone, methyl or ethyl alcohol or hot water, sparingly in cold water or mineral acids and insoluble in ether, benzene or ethyl acetate. In many cases they yield brominated phenols on treatment with bromine, the arsenic being entirely split off. With mild reducing agents, such as sodium amalgam in methyl alcoholic solution or sodium hydrosulfite at 0°, they yield aminohydroxyarsonic acids; with stronger reagents, e. g., hypophosphorous acid or stannous chloride-hydrochloric acid at low temperature, dinitrodihydroxyarseno compounds are obtained, while upon more intense reduction, as with sodium hydrosulfite at 50-60°, the products are diaminodihydroxyarseno derivatives.

The O-substituted derivatives may be obtained either like the unsubstituted compounds or from the latter by the methods usually employed in the preparation of similar phenolic compounds.

4-Nitro-2-hydroxyphenylarsonic acid, $H_2O_3AsC_6H_3\begin{matrix} \diagup OH \\ \diagdown NO_2 \end{matrix}$, is made by Bart's method from 3-nitro-6-aminophenol, and isolated through its magnesium salt. It separates from hot water as crystals decomposing at 250°, and readily soluble in water, glacial acetic acid, acetone, methyl or ethyl alcohol. The nitro group may be reduced with iron filings and dilute acetic acid.[1164]

5-Nitro-2-hydroxyphenylarsonic acid is prepared from 1-amino-2-hydroxy-5-nitrobenzene by Bart's reaction;[86] or by warming 4-nitroanilinearsonic acid with concentrated caustic potash solution at 90-5°, and isolating the acid through its potassium salt[1165] in the form of amber-colored crystals readily soluble in ammonia, caustic alkalis, sodium carbonate or acetate, acetone, acetic acid, hot water, methyl or ethyl alcohol, sparingly soluble in the latter three solvents when cold and insoluble in ether. It melts with decomposition at 247-8°, and may be reduced by means of sodium hydrosulfite to the corresponding diamino arseno compound.

2-Nitro-3-hydroxyphenylarsonic acid is obtained by heating 2-nitro-3-aminophenylarsonic acid with concentrated potassium hydroxide solution. It may be reduced to the arseno compound as above.[724]

3-Nitro-4-hydroxyphenylarsonic acid is of considerable practical importance, as it is the final intermediate product in the preparation of

arsphenamine base. It may be produced in a variety of ways—144 g. of dry monosodium-4-hydroxyphenylarsonate is dissolved in 450 c.c. of concentrated sulfuric acid at low temperature and treated with a mixture of 39 c.c. of nitric acid (d, 1.4) and 39 c.c. of concentrated sulfuric acid at 0°. After allowing to stand for several hours at 10°, and subsequently pouring into 2250 c.c. of cold water, the whole is again allowed to stand for 24-48 hours, whereupon the product separates out. This is filtered, washed free of sulfuric acid with a saturated sodium chloride solution, and the latter removed with water.[1166]

By another method 3-nitro-4-aminophenylarsonic acid is warmed with concentrated caustic potash at 80° until it can no longer be diazotized. The solution is then diluted with water, enough hydrochloric acid added so that it does not react alkaline to turmeric and finally filtered. On acidifying the solution with an excess of hydrochloric acid and allowing to stand for 24 hours, the nitro acid separates out.[1167]

A third method consists in heating a solution of 500 g. of 3-nitro-4-dimethylaminophenylarsonic acid in aqueous caustic potash (500 g. of potash in 1500 c.c. of water) at 80-90° until the mixture becomes almost solid. Two liters of ice water followed by concentrated hydrochloric acid are then added, the resulting precipitate dissolved in hot water, filtered, and the liquid treated with sodium acetate and animal charcoal. The final product separates on acidifying the filtrate with hydrochloric acid.[1168] A similar procedure for obtaining the compound, using caustic soda instead of potash, has also been described.[614]

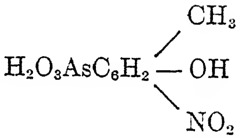
According to a fourth method, a solution of 3-nitro-4-methoxyphenylarsonic acid in 15 per cent aqueous soda is heated on a water-bath, and subsequently treated with hydrochloric acid.[1169]

Finally, the desired arsonic acid is formed upon treating o-nitro-p-aminophenol either according to Bart's original method [86] or Mouneyrat's modification thereof.[89]

When recrystallized from water the acid separates either in tufts of almost colorless needles, or yellow, rhombohedral plates which deflagrate on heating, are readily soluble in methyl or ethyl alcohol, glacial or 50 per cent acetic acid, acetone or alkali, sparingly soluble in cold water, less soluble in dilute mineral acids and insoluble in ether or ethyl acetate. It is moderately soluble in hot water with a yellow color which almost entirely disappears upon the addition of mineral acids. With sodium amalgam in methyl alcoholic medium or sodium hydrosulfite at 0°, it yields 3-amino-4-hydroxyphenylarsonic acid; with hypophosphorous acid in aqueous medium or with stannous chloride-hydrochloric acid in methyl alcoholic solution at low temperature there is formed 3,3′-dinitro-4-,4′-dihydroxyarsenobenzene, while with sodium hydrosulfite at 55-60°, 3,3′-diamino-4,4′-dihydroxyarsenobenzene is obtained.

The acid forms three series of salts with alkalis—a mono-, di- and

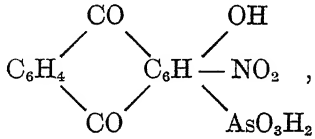
trimetallic salt, depending on whether one, two or three molecular proportions of alkali are employed. They are all precipitated from solution by alcohol. The aqueous solution of the pale yellow monosodium salt has an acid reaction, and yields the corresponding sesquisulfide with hydrogen sulfide, but an unidentified brown product with sodium sulfide in alkaline solution.[1170] The disodium salt is orange and has a neutral reaction, while the trisodium salt exists in two forms, colored orange and beautiful red respectively, the latter probably possessing a *quinoid aci* formula.[466] Both varieties may be easily converted one into the other—the red into the orange modification by simply heating in the dry state, and the orange into the red compound by warming with alcohol in the presence of an excess of alkalis. The aqueous solutions of both varieties react alkaline to litmus and neutral to phenolphthalein.

3-Nitro-4-hydroxy-2-methylphenylarsonic acid,  ,

results on nitrating 4-hydroxy-2-methylphenylarsonic acid with one molecular proportion of nitric acid. When warmed with concentrated aqueous sodium hydroxide no stilbene compound is formed.[1171]

5-Nitro-4-hydroxy-3-methylphenylarsonic acid is prepared by nitrating o-cresolarsonic acid;[1172] or by warming either 3-nitro-4-amino-5-methylphenylarsonic acid[1173, 425] or 3-nitro-4-chloro-5-methylphenylarsonic acid[907] with concentrated alkali. When crystallized rapidly from boiling water it forms clusters of slender, yellow needles, but on crystallizing slowly from 50 per cent acetic acid, there are obtained well-defined rhombic prisms. Both varieties decompose at 310° with explosive violence.

3-Nitro-4-hydroxyanthraquinonearsonic acid,

 ,

is obtained by dissolving 4-hydroxyanthraquinonearsonic acid in sulfuric acid monohydrate and nitrating with a nitric-sulfuric acid mixture at 0-5°. It crystallizes from boiling glacial acetic acid as yellow needles decomposing indefinitely at about 230°, and turning red in contact with even traces of alkalis. The compound is almost insoluble in water, methyl or ethyl alcohol, slightly soluble in boiling glacial acetic acid, dissolves in concentrated sulfuric acid to a yellow solution, and forms a red solution with dilute aqueous alkali, sodium carbonate or acetate. When sodium

amalgam is added to the red alkaline solution it gradually turns violet; on acidulating this solution brownish-violet flakes are precipitated.[1174]

3,5-Dinitro-2-hydroxyphenylarsonic acid, $H_2O_3AsC_6H_2\begin{matrix}\diagup (NO_2)_2\\ \diagdown OH\end{matrix}$, is made by nitrating 5-nitro-2-hydroxyphenylarsonic acid at 0-5°, and crystallizes from hot water in pale yellow needles, m. p. 237°. Its alkaline solution has a deeper yellow color than the mononitro compound, from which it is distinguished by the deep red coloration produced by a very small amount of sodium hydrosulfite added to its alkaline solution.[723]

3,5-Dinitro-4-hydroxyphenylarsonic acid results either upon nitrating 4-hydroxyphenylarsonic acid with an excess of nitric acid (d, 1.52) at 15-20°,[1172] or upon heating 3,5-dinitro-4-aminophenylarsonic acid with 10 per cent caustic potash solution.[1175] It forms yellow, rhombohedral plates which deflagrate on heating and are readily soluble in hot water or methyl alcohol. Its aqueous solution has a deeper color than that of the 3-nitrohydroxy acid, and it may be detected in the presence of the latter by the deep red coloration produced upon adding a small amount of sodium hydrosulfite to an alkaline solution of the mixture. The yellow color it imparts to wool is more intense than that imparted by the preceding isomer. Heating with 40-50 per cent caustic potash at 90-100° decomposes it with the evolution of ammonia.

Its sodium salt forms yellow needles; the potassium salt consists of orange-red crystals.

3,5-Dinitro-4-hydroxy-2-methylphenylarsonic acid,

$$H_2O_3AsC_6H\begin{matrix}\diagup (NO_2)_2\\ -OH\\ \diagdown CH_3\end{matrix},$$

obtained by nitrating 4-hydroxy-2-methylphenylarsonic acid with 2 moles of nitric acid in concentrated sulfuric acid medium, crystallizes from water as hydrous yellow needles which turn white on dehydration. When warmed with concentrated aqueous caustic soda it yields a stilbene dye.[591]

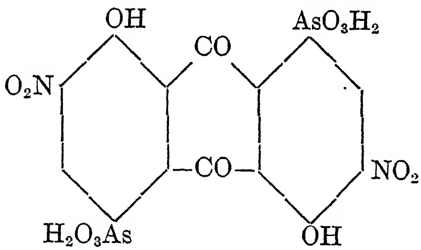
5-Nitro-2,4-dihydroxyphenylarsonic acid, $H_2O_3AsC_6H_2\begin{matrix}\diagup (OH)_2\\ \diagdown NO_2\end{matrix}$,

which results upon nitrating the corresponding dihydroxyarsonic acid below 0°, crystallizes from water in the form of pale yellow needles containing $2H_2O$. The anhydrous compound is colorless, melts at 223° with decomposition, is readily soluble in alcohol, glacial acetic acid or hot water, sparingly soluble in cold water and insoluble in ether or benzene. With ferric chloride solution it yields a red coloration. With bromine in glacial acetic acid the arsenic is split off, 2,6-dibromo-4-nitroresorcinol being formed.[1149]

3,5-Dinitro-2,4-dihydroxyphenylarsonic acid, $H_2O_3AsC_6H\begin{matrix} \diagup\!\!\!\diagup (NO_2)_2 \\ \diagdown\!\!\!\diagdown (OH)_2 \end{matrix}$,

results on nitrating resorcinolarsonic acid at 60°. It separates from water as yellow crystals melting with decomposition at 206°, soluble in water, alcohol or acetone, but less so in glacial acetic acid. It gives a deep orange color with ferric chloride, while with bromine in alcoholic solution, 2,4-dinitro-6-bromoresorcinol results.[1176]

3,7-Dinitro-4,8-dihydroxyanthraquinone-1,5-diarsonic acid,



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is formed upon treating 4,8-dihydroxyanthraquinonediarsonic acid with a nitrating mixture at 16-20°, warming at 25-30° for four hours, then raising the temperature to 80°, and finally precipitating in water. It is a greenish-yellow, microcrystalline powder which is soluble in concentrated sulfuric acid, N-caustic soda or 2N-sodium carbonate, difficultly so in water, methyl or ethyl alcohol and insoluble in N-hydrochloric or glacial acetic acid. Sodium amalgam changes the yellowish-red color of its alkaline solution to violet, the diamino compound being formed, while with sodium hydrosulfite the same alkaline solution yields a red vat-dye which on exposure to air becomes bright blue. On the other hand, when a hot solution of the acid in sodium acetate is treated with sodium hydrosulfite there is obtained a brownish-violet precipitate which dissolves in caustic alkalis with a blue color.

The disodium salt is a violet powder soluble in water or 50 per cent acetic acid but insoluble in methyl or ethyl alcohol. With N-caustic

soda it forms a yellowish-red solution from which alcohol precipitates a beautiful bluish-red salt.[1177]

5,5′-Dinitro-4,4′-dihydroxy-2,2′-stilbenediarsonic acid,

$$\begin{array}{ccccc} & H_2O_3As & & AsO_3H_2 & \\ & \diagdown & & \diagup & \\ O_2N - & C_6H_2.CH = & & HC.C_6H_2 & - NO_2 \\ & \diagup & & \diagdown & \\ & HO & & OH & \end{array},$$

results upon warming 4,4′-dichloro-5,5′-dinitro-2,2′-stilbenediarsonic acid with sodium hydroxide and sodium hypochlorite solutions on a water-bath for several hours.[730]

4-Nitro-2-methoxyphenylarsonic acid, $H_2O_3AsC_6H_3\begin{array}{l}\diagup NO_2 \\ \diagdown OCH_3\end{array}$, prepared from 4-nitro-o-anisidine by Bart's method, crystallizes from 90 per cent alcohol in pale yellow needles which do not melt below 250°.[151]

3-Nitro-4-methoxyphenylarsonic acid may be produced by nitrating 4-methoxyphenylarsonic acid at — 8° to 0° and precipitating the product with ice;[1169, 1178] by methylating 3-nitro-4-hydroxyphenylarsonic acid;[1179] or by treating 4-methoxy-m-nitroaniline according to Mouneyrat's modification of Bart's method.[89] It forms yellowish-white crystals sparingly soluble in cold water, though more so on heating, slightly soluble in methyl alcohol, and dissolving in alkalis to form yellowish salts. The acid begins to decompose above 290°.

3-Nitro-4-ethoxyphenylarsonic acid, $H_2O_3AsC_6H_3\begin{array}{l}\diagup NO_2 \\ \diagdown OC_2H_5\end{array}$, can be made by either nitrating 4-ethoxyphenylarsonic acid,[1169] or from 4-ethoxy-m-nitroaniline by Mouneyrat's modification of Bart's method.[89]

3-Nitro-4-methoxy-5-methylphenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{array}{l}\diagup NO_2 \\ - OCH_3. \\ \diagdown CH_3\end{array}$$

Pale yellow needles obtained by nitrating 4-methoxy-5-methylphenylarsonic acid, allowing the temperature to rise to 15° and precipitating in water.[1180]

(3-Nitrophenyl-4-arsonic acid) hydroxyacetic acid,

$$(H_2O_3As)(O_2N)C_6H_3OCH_2COOH,$$

is made by nitrating the corresponding arsonic acid in the usual way, allowing the temperature to rise to 20° and precipitating in water. It forms coarse yellow prisms very soluble in hot water but quite difficultly so in cold.[1180]

p-Toluenesulfonic acid ester of 3-nitro-4-hydroxyphenylarsonic acid, $CH_3.C_6H_4SO_2.O.C_6H_3(NO_2)AsO_3H_2$, is prepared by dissolving 3-nitro-4-hydroxyphenylarsonic acid in dilute sodium carbonate solution, digesting with p-toluenesulfonic chloride at 70°, and precipitating in ice cold dilute hydrochloric acid. It consists of bright, lustrous leaflets, m. p. 171°; readily soluble in caustic alkalis, aqueous sodium bicarbonate, methyl or ethyl alcohol, warm acetone or glacial acetic acid, sparingly so in ethyl acetate and practically insoluble in water. It can be readily diazotized.[1181]

5-Nitro-4-acetoxy-3-methylphenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{array}{l} \diagup NO_2 \\ -CH_3 \\ \diagdown O.COCH_3 \end{array},$$

is obtained by acetylating the corresponding hydroxyarsonic acid with acetic anhydride in the presence of a trace of pyridine. It exists as colorless, spherical, anhydrous nodules fairly readily soluble in methyl or ethyl alcohol or boiling water, but only sparingly in cold water or ethyl acetate.[1182]

5-Nitro-4-methoxy-3-hydroxyphenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{array}{l} \diagup NO_2 \\ -OH \\ \diagdown OCH_3 \end{array},$$

formed upon nitrating the corresponding arsonic acid, crystallizes from water, in which it is sparingly soluble, in stellate clusters of prismatic needles melting at 252° with preliminary darkening. Reduction with warm hypophosphorous acid yields the corresponding arseno compound, but with sodium hydrosulfite there is formed a brick red substance which contains two atoms of arsenic attached to each benzene nucleus, and whose exact structure has not been definitely ascertained.[624]

5-Nitro-2-methoxy-4-hydroxyphenylarsonic acid is formed on nitrating 2-methoxy-4-hydroxyphenylarsonic acid with nitric-glacial acetic

acids in glacial acetic acid medium. It forms pale yellow scales sparingly soluble in water, methyl or ethyl alcohol or glacial acetic acid.[625]

5-Nitro-3-methoxy-4-hydroxyphenylarsonic acid is made by nitrating the 3-methoxy-4-hydroxy compound in the usual way, and neutralizing the bulk of the mineral acid with anhydrous soda. It crystallizes from hot water as glistening leaflets which decompose gradually above 260° without melting. Warming with dilute hypophosphorous acid produces the corresponding nitroarseno compound, but hydrosulfite in alkaline solution reduces the nitro group as well.[631]

5-Nitro-2,4-dimethoxyphenylarsonic acid, $H_2O_3AsC_6H_2\begin{matrix}\diagup (OCH_3)_2 \\ \diagdown NO_2\end{matrix}$.

—Feathery needles with a slight tinge of greenish yellow, which are produced by nitrating the dimethoxyarsonic acid.[1180]

5-Nitro-3,4-dimethoxyphenylarsonic acid is prepared by nitrating the corresponding dimethoxy acid at low temperature, and may be crystallized from boiling water in clusters of minute needles melting with decomposition at 236°. On heating with concentrated hydrochloric acid at 130°, hydrolysis of the methoxy groups occurs, whereas boiling with the same reagent at 160° decomposes the compound.

The monosodium salt crystallizes with $6H_2O$ as glistening, flattened prisms which lose their luster when dried in air, while the acid barium salt crystallizes with only three molecules of water in the form of faintly yellow needles.[627]

5-Chloro-3-nitro-4-hydroxyphenylarsonic acid, $H_2O_3AsC_6H_2\begin{matrix}\diagup Cl \\ — NO_2 \\ \diagdown OH\end{matrix}$,

is produced by nitrating 5-chloro-4-hydroxyphenylarsonic acid at 0°. On reduction with sodium hydrosulfite it yields the corresponding arseno compound.[1183]

5-Iodo-3-nitro-4-hydroxyphenylarsonic acid is obtained by adding an aqueous solution of iodine and potassium iodide in small portions to an aqueous suspension of 5-acetoxymercuri-3-nitro-4-hydroxyphenylarsonic acid contained in a glass-stoppered bottle, which is vigorously shaken after each addition until the color of the iodine is completely discharged. The mixture is then filtered and precipitated with dilute sulfuric acid. The product is a very hygroscopic, light yellow powder insoluble in water, alcohol or ether but soluble in acetone, dilute sodium hydroxide or carbonate solution.[1184]

17. *Amino Hydroxy Aryl Arsonic Acids.*—The members of this group are obtained:

1. By reducing the corresponding nitro acids with nascent hydrogen (from sodium amalgam and methyl alcohol, iron filings and dilute acetic acid, sodium hydrosulfite at 0°, or by electrolysis).

2. From nitroaminoarsonic acids, in which the NO_2 and NH_2 groups are in ortho position to each other, by diazotizing with sodium nitrite, replacing the NO_2 by an OH with sodium acetate, coupling with an azo component like β-naphthol, and reducing the resulting dye with either sodium hydrosulfite or aluminium powder:

$$H_2O_3AsC_6H_3\left\langle\begin{array}{l}NO_2\\ \\ NH_2\end{array}\right. \longrightarrow H_2O_3AsC_6H_3\left\langle\begin{array}{l}NO_2\\ \\ N=NX\end{array}\right. \longrightarrow$$

$$H_2O_3AsC_6H_3\left\langle\begin{array}{l}OH\\ \\ N=NX\end{array}\right. \longrightarrow H_2O_3AsC_6H_3\left\langle\begin{array}{l}OH\\ \\ N=N.C_{10}H_6OH\end{array}\right. \longrightarrow$$

$$H_2O_3AsC_6H_3\left\langle\begin{array}{l}OH\\ \\ NH_2\end{array}\right. + C_{10}H_6\left\langle\begin{array}{l}OH\\ \\ NH_2\end{array}\right. .$$

3. Upon oxidizing diaminodihydroxyarsenobenzenes with hydrogen peroxide or iodine in alkaline solution:

$$\left.\begin{array}{r}H_2N\\ \\ HO\end{array}\right\rangle RAs=AsR\left\langle\begin{array}{l}NH_2\\ \\ OH\end{array}\right. + 2O_2 + 2H_2O \longrightarrow 2R\begin{array}{l}\diagup AsO_3H_2\\ -NH_2\\ \diagdown OH\end{array} .$$

4. By similarly oxidizing the corresponding arsineoxides:

$$\left.\begin{array}{r}H_2N\\ \\ HO\end{array}\right\rangle RAsO + O + H_2O \longrightarrow R\begin{array}{l}\diagup AsO_3H_2\\ -NH_2\\ \diagdown OH\end{array} .$$

The amino hydroxy arsonic acids are generally crystalline solids soluble in excess of dilute alkalis or mineral acids, more or less soluble in water, methyl or ethyl alcohol and generally insoluble in the other

organic solvents. They may be reduced to the arsineoxides by sulfur dioxide in the presence of a slight amount of hydriodic acid as a catalyst, while stronger reducing agents, like sodium hydrosulfite, reduce them to the corresponding diamino dihydroxy arsenobenzenes. The alkaline solutions of 3-amino-4-hydroxy- and 3,5-diamino-4-hydroxyphenylarsonic acids darken on exposure to air, and also reduce ammoniacal silver solution.

The N-substituted derivatives may be prepared from the amino acids by the methods usually employed with ordinary amines; by reducing the corresponding nitro acids; from the corresponding substituted aminophenols by the Béchamp reaction; or by applying Bart's reaction or Mouneyrat's modification of same to N-monosubstituted diaminophenols. They are generally crystalline compounds soluble in alkalis. Mineral acids dissolve all of the alkylated, and some of the acylated derivatives.

The O-substituted derivatives, prepared by reducing the corresponding nitro acids, are crystalline, water-soluble products which behave like arsonic acids, amines and substituted phenols.

Although the free amino hydroxy arsonic acids themselves cannot be nitrated, their N- or O-substituted derivatives, or those compounds containing substituents in both the amino and hydroxyl groups, can be readily converted into the corresponding nitro derivatives, which upon hydrolysis yield either nitro amino hydroxy- or o-substituted nitro amino hydroxy arsonic acids.

4-Amino-2-hydroxyphenylarsonic acid, $H_2O_3AsC_6H_3{<}^{OH}_{NH_2}$, may be prepared either by reducing the corresponding nitro acid with iron filings and dilute acetic acid;[1164] or by boiling the corresponding carbethoxy compound with dilute caustic soda solution and precipitating with sulfuric acid.[639] The product is readily soluble in water, methyl or ethyl alcohol, sparingly in acetone and insoluble in ether or hydrocarbons. It melts at 173°, and yields the carbethoxy derivative when treated with ethyl chlorocarbonate.

4-Amino-3-hydroxyphenylarsonic acid is obtained by diazotizing 3-nitro-4-aminophenylarsonic acid, treating with sodium acetate solution, and warming the mixture at 18° until coupling with R-salt no longer occurs. The diazo solution is then coupled with alkaline β-naphthol and the resulting azo dye isolated by neutralizing with hydrochloric acid and saturating with sodium chloride. The azo compound is now reduced with sodium hydrosulfite in alkaline solution, the precipitate of 1-amino-2-naphthol filtered off, and the excess hydrosulfite in the filtrate oxidized by a current of air. The liquid is then con-

centrated and neutralized with sulfuric acid, whereupon the amino hydroxy arsonic acid separates as a fine, crystalline powder. Instead of reducing the above azo compound with sodium hydrosulfite, aluminium powder may be used in alkaline solution at 40-60°.

The acid is readily soluble in alkali hydroxides or carbonates, ammonia, sodium acetate or an excess of dilute mineral acids, sparingly so in cold water or alcohol and insoluble in ether. With sodium hypochlorite in alkaline solution a green coloration results, but in acid solution the coloration is dull red. On reduction with an excess of sodium hydrosulfite the corresponding arseno compound is obtained.

The monosodium salt, $(H_2N)(HO)C_6H_3AsO_3HNa.5H_2O$, consists of lustrous scales readily soluble in water. On adding silver nitrate to its aqueous solution there separates a white, curdy precipitate of the silver salt which dissolves in ammonia or nitric acid. Magnesia mixture in ammoniacal solution produces a precipitate only upon warming.[1185]

3-Amino-4-hydroxyphenylarsonic acid may be produced in a number of ways. A solution of the corresponding nitro hydroxy acid in methyl alcohol is treated with sodium amalgam until the evolution of hydrogen ceases, and after distilling off the alcohol the residue is taken up with water, separated from the metallic mercury and treated with an excess of hydrochloric acid. The next day the impurities are removed by filtration, the liquid boiled with charcoal and rendered neutral to congo with caustic soda. The precipitation of the amino derivative is then completed by the addition of acetic acid.[1186]

Other methods of reduction consist in subjecting an alkaline solution of the 3-nitro-4-hydroxy acid to electrolysis,[1169] boiling with ferrous sulfate,[947] or treatment with sodium hydrosulfite in the presence of magnesium chloride at 0°.[1187] The same product may also be obtained by oxidizing either an alkaline solution of arsphenamine base with hydrogen peroxide at low temperature,[1188] or an aqueous solution of arsphenamine with iodine solution.[1189]

The pure acid exists as practically colorless prisms readily soluble in excess of alkalis or mineral acids, sparingly in water, insoluble in the usual organic solvents, and decomposing at about 290° with preliminary darkening and softening. Its alkaline solution becomes dark brown on exposure to air; with alkaline hypochlorite solution it yields a deep green coloration, while the addition of a drop of potassium bichromate solution to a dilute mineral acid solution of the amino hydroxy acid produces a beautiful red color. Furthermore, the acid reduces ammoniacal silver solution, slowly in the cold but more readily upon warming, and is itself reduced to the corresponding arsineoxide by the action of sulfurous acid in the presence of hydriodic acid. The monosodium salt crystallizes with one or two molecules of water, and is readily soluble in water.

3-Amino-4-hydroxy-5-methylphenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{array}{l} / \ CH_3 \\ — NH_2, \\ \backslash \ OH \end{array}$$

is prepared by reducing the corresponding nitro acid with sodium hydrosulfite in alkaline solution. It is soluble in water, and may be salted out from aqueous solution by means of sodium chloride.[1190]

3-Amino-4-hydroxyanthraquinonearsonic acid,

$$C_6H_4\begin{array}{c} / \ CO \ \backslash \\ \\ \backslash \ CO \ / \end{array}C_6H\begin{array}{l} / \ AsO_3H_2 \\ — NH_2 \\ \backslash \ OH \end{array},$$

is made by reducing the corresponding nitro derivative with sodium amalgam at 65°, and is purified through its sodium salt. It separates as violet, silky crystals melting indefinitely at about 265°, readily soluble in ammonia, N-caustic soda, 2N-soda, concentrated sulfuric or hot 5N-hydrochloric acid, and in boiling 2N-sodium acetate solution, difficultly soluble in glacial acetic acid and insoluble in water, alcohol or N-hydrochloric acid. On adding alcohol to its alkaline solution there separates a blue-violet sodium salt which dissolves in water with a fuchsin red color, while with magnesia mixture in ammoniacal solution a red-violet precipitate is formed. The acid may be diazotized, and the resulting diazo compound coupled with alkaline solutions of R-salt or resorcin, yielding violet and blue colorations respectively. On treating the alkaline solution of the arsonic acid with sodium hydrosulfite there is formed an orange-colored vat-dye which immediately turns violet on filter paper.[1191]

5-Amino-2,4-dihydroxyphenylarsonic acid, $H_2O_3AsC_6H_2\begin{array}{l} // \ (OH)_2 \\ \\ \backslash \ NH_2 \end{array}$,

obtained by reducing the corresponding nitro compound with sodium hydrosulfite, forms aggregates of needles containing one molecule of water of crystallization. It is soluble in alkalis or mineral acids but very sparingly in water, glacial acetic acid, acetone, methyl or ethyl alcohol. Its alkaline solution turns blue on exposure to air due to the formation of an indophenol dye. The amino acid reduces ammoniacal silver nitrate at ordinary temperatures, and can be readily diazotized, yielding a blue-red compound when coupled with resorcin.[1192]

3,5-Diamino-4-hydroxyphenylarsonic acid, $H_2O_3AsC_6H_2\begin{cases}(NH_2)_2\\(OH)\end{cases}$,

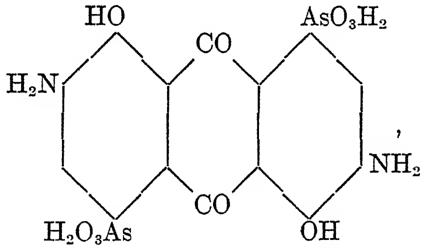
is formed upon reducing the corresponding dinitro compound with sodium hydrosulfite at low temperature. It crystallizes in white needles which darken during purification, are decomposed above 170° without melting, dissolve in alkalis or dilute mineral acids but not in methyl or ethyl alcohol, ether, acetone, chloroform or benzene. Its alkaline solution darkens on exposure to air.[1193]

3,5-Diamino-2,4-dihydroxyphenylarsonic acid,

$$H_2O_3AsC_6H\begin{cases}(NH_2)_2\\(OH)_2\end{cases}.$$

In this case the reduction of the corresponding dinitro dihydroxy acid is effected by means of stannous chloride and hydrochloric acid at 35-40°.[635]

3,7-Diamino-4,8-dihydroxyanthraquinone-1,5-diarsonic acid,



is produced by reducing an alkaline solution of the corresponding dinitro compound with sodium amalgam at 55°, and purifying through its sodium salt. The diarsonic acid is a dark brown to black-violet powder with a metallic luster, soluble in concentrated sulfuric acid, ammonia, 2N-soda or N-sodium hydroxide, almost insoluble in boiling water or glacial acetic acid and completely so in methyl or ethyl alcohol. When its sulfuric acid solution is strongly diluted with water, and the suspension of the precipitated red-violet flakes treated with sodium nitrite, a wine red diazo solution is obtained which couples green with a solution of resorcin in soda. The ammoniacal solution of the acid gives a blue-violet precipitate with magnesia mixture, and one of pure blue with calcium chloride. With sodium hydrosulfite in alkaline solution there is formed an orange-yellow vat-dye, which becomes red-violet on exposure to air.[1194]

4-Acetylamino-3-hydroxyphenylarsonic acid,

$$\mathrm{H_2O_3AsC_6H_3}\begin{matrix} \diagup\ \mathrm{OH} \\ \diagdown\ \mathrm{NH.COCH_3} \end{matrix},$$

prepared by acetylating the corresponding amino acid, forms colorless needles easily soluble in hot methyl alcohol, water, N-hydrochloric acid, sodium carbonate or acetate solution but difficultly soluble in cold N-hydrochloric acid. It hydrolyzes on boiling.[1195]

3-Acetylamino-4-hydroxyphenylarsonic acid is an almost colorless, crystalline substance soluble in dilute alkalis but insoluble in hydrochloric or acetic acid or the usual organic solvents.[1196]

3,5-Di(acetylamino)-4-hydroxyphenylarsonic acid,

$$\mathrm{H_2O_3AsC_6H_2}\begin{matrix} \diagup\ \mathrm{OH} \\ \diagdown\!\!\diagdown\ \mathrm{(NH.COCH_3)_2} \end{matrix},$$

is a pale brown, crystalline substance soluble in alkalis but insoluble in water, mineral acids or the usual organic solvents. It is prepared by acetylating the corresponding diamino acid.[633]

5-Acetylamino-2,4-dihydroxyphenylarsonic acid,

$$\mathrm{H_2O_3AsC_6H_2}\begin{matrix} \diagup\!\!\diagup\ \mathrm{(OH)_2} \\ \diagdown\ \mathrm{NH.COCH_3} \end{matrix},$$

similarly prepared, is soluble in water or concentrated hydrochloric acid but sparingly in the usual organic solvents.[634]

4-Carbethoxyamino-2-hydroxyphenylarsonic acid,

$$\mathrm{H_2O_3AsC_6H_3}\begin{matrix} \diagup\ \mathrm{OH} \\ \diagdown\ \mathrm{NH.COOC_2H_5} \end{matrix},$$

may be obtained either by treating 4-amino-2-hydroxyphenylarsonic acid with ethyl chlorocarbonate in alkaline solution,[1164] or by heating 3-carbethoxyaminophenol with arsenic acid on the water-bath for a week, and isolating the product through the ammonium salt.[1197] The acid melts with decomposition at 213°, is readily soluble in methyl

or ethyl alcohol, glacial acetic acid, concentrated hydrochloric acid or hot water, but sparingly in cold water, acetone, benzene or ether. On boiling with concentrated sodium hydroxide solution the carbethoxy group is split off.

3-Carbethoxyamino-4-hydroxyphenylarsonic acid is produced from 3-amino-4-hydroxyphenylarsonic acid and ethyl chlorocarbonate as in the preceding isomer,[638] or from 1-amino-3-carbethoxyamino-4-hydroxybenzene either by Bart's method,[1144] or Mouneyrat's modification.[89] The product may be recrystallized from water, and dissolves in alkalis, methyl or ethyl alcohol, but is insoluble in acids, ether or benzene.

3-Carbamido-4-hydroxyphenylarsonic acid,

$$\mathrm{H_2O_3AsC_6H_3}\begin{array}{l}\diagup\,\mathrm{OH}\\ \diagdown\,\mathrm{NH.CONH_2}\end{array},$$

results upon treating an alkaline solution of 3-amino-4-hydroxyphenylarsonic acid with potassium cyanate and glacial acetic acid, and allowing the mixture to stand over night. The product is then precipitated by adding hydrochloric acid.[638]

3-Methylamino-4-hydroxyphenylarsonic acid,

$$\mathrm{H_2O_3AsC_6H_3}\begin{array}{l}\diagup\,\mathrm{OH}\\ \diagdown\,\mathrm{NH.CH_3}\end{array},$$

separates on treating an alkaline solution of the amino hydroxy acid with dimethylsulfate (0.5 mole), and subsequently acidifying with a mixture of hydrochloric and acetic acids. It crystallizes from water with $\frac{1}{2}H_2O$ in fan-shaped groups of needles melting with decomposition at 263-263.5°, easily soluble in methyl or ethyl alcohol, 50 per cent or hot glacial acetic acid, readily in water, alkalis or aqueous mineral acids, slightly in acetone and insoluble in ether. Its aqueous solutions must be concentrated in vacuo and at low temperature as otherwise decomposition occurs.[1198]

4-Dimethylamino-2-hydroxyphenylarsonic acid,

$$\mathrm{H_2O_3AsC_6H_3}\begin{array}{l}\diagup\,\mathrm{OH}\\ \diagdown\,\mathrm{N(CH_3)_2}\end{array},$$

is obtained from 4-dimethylamino-2-nitrophenylarsonic acid by simply heating with 40% sulfuric acid and subsequently rendering almost neutral with sodium carbonate; by treating the sulfuric acid solution of the same nitro compound with either copper powder or urea; or by warming its alkaline solution with ferrous sulfate. The product is easily soluble in water, dilute alkalis and in very dilute sulfuric or acetic acid.[1199]

3-Dimethylamino-4-hydroxyphenylarsonic acid is prepared by treating an alkaline solution of the amino hydroxy compound with two moles of dimethylsulfate. It separates from water as compact crystals which when dried in a desiccator change to a delicate, faintly colored, crystalline powder very easily soluble in methyl alcohol, easily soluble in hot water, alcohol, glacial or 50% acetic acid, alkalis or aqueous mineral acids, moderately so in cold water, sparingly in acetone and insoluble in ether. On rapid heating it softens at about 119° and melts with foaming at 119-21°, turning reddish-brown at the same time.[1200]

3-Trimethylammonium-4-hydroxyphenylarsonic acid,

$$H_2O_3AsC_6H_3\begin{cases}(OH)\\ N(CH_3)_3(OH)\end{cases}.$$

3-Amino-4-hydroxyphenylarsonic acid (21 g.) is shaken with methyl alcohol (210 c.c.), 10N-sodium hydroxide (9 c.c.) and methyl iodide (6 c.c.). After several hours a second addition of the same quantities of alkali and methyl iodide is made, and the next day a third. Finally, the methyl alcohol is distilled off, and after adding glacial acetic acid and alcohol to the residue, the whole is permitted to stand for 24 hours, during which time a crystalline precipitate deposits. This consists of a mixture of the desired ammonium hydroxide derivative and the quaternary iodide, which are separated by recrystallizing the crude product from water, the more soluble iodide remaining in the mother liquor, while the pure acid separates out as shining, vitreous prisms melting with decomposition at 262-4°. It is easily soluble in glacial or 50% acetic acid, aqueous alkalis or mineral acids, moderately soluble in water with an acid reaction to litmus, sparingly in methyl alcohol and still less soluble in ethyl alcohol or acetone. When warmed for some time at 110-14° the acid loses one molecule of water, forming an inner anhydride, $H_2O_3AsC_6H_3\begin{cases}N(CH_3)_3\\ \quad\big|\\ O\end{cases}$.[1201]

4-Amino-2-methoxyphenylarsonic acid, $H_2O_3AsC_6H_3(NH_2)(OCH_3)$, from the corresponding nitro acid by reduction with ferrous chloride in alkaline solution, crystallizes from water in white needles melting with decomposition at 203-4°, when heated slowly, and at 208-9° when the heating is rapid. It condenses with benzaldehyde and pyruvic acid, forming 1-(4′-arsono-3′-methoxyphenyl)-2-phenyl-4,5-diketopyrrolidine.[151]

4-Amino-3-methoxyphenylarsonic acid (o-Anisidine-4-arsonic acid). —The azo dye obtained from 3-nitro-4-aminophenylarsonic acid (as described under the preparation of 4-amino-3-hydroxyphenylarsonic acid) is ground together with calcined soda, refluxed with methyl toluene-p-sulfonate and methyl alcohol, and the resulting methylated azo derivative finally reduced with alkaline hydrosulfite. The desired product is obtained as long, colorless, shiny needles easily soluble in alkalis, mineral or 50% acetic acid, sodium acetate or hot water. Its diazo-derivative is colorless, coupling with R-salt to a blue-red coloration.[1202]

3-Amino-4-methoxyphenylarsonic acid results upon reducing the corresponding nitro derivative with sodium amalgam in methyl alcohol medium, separating as clusters of colorless needles melting with decomposition at 193°.[1203]

2,4-Diamino-3-methoxyphenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{cases}(NH_2)_2\\ OCH_3\end{cases},$$

is made by reducing an alkaline solution of 2-nitro-4-amino-3-methoxyphenylarsonic acid with ferrous chloride, and isolating as the white, pulverulent magnesium salt which is hardly soluble in water, but very easily so in dilute mineral acids. The latter solution becomes intensely yellow on the addition of sodium nitrite, and then couples with R-salt to a red, and with resorcin to an orange-colored solution. With 4-nitrodiazobenzene in acetic acid solution the above arsonic acid yields a yellow-red arsenical dye which dissolves in 2N-sodium carbonate with an orange-red color (distinction from the succeeding isomer), while with diazosulfanilic acid there is also obtained an arsenical dye soluble in soda solution.[1204]

4,6-Diamino-3-methoxyphenylarsonic acid is similarly prepared from 6-nitro-4-amino-3-methoxyphenylarsonic acid. It crystallizes in colorless, felted needles very easily soluble in alkalis, sodium acetate solution, dilute mineral acids and in hot glacial or 50% acetic acid, easily soluble in hot but difficultly in cold alcohol. Its diazo solution couples

intensely blue-red with R-salt, and orange with resorcin. When treated with 4-nitrodiazobenzene in acetic acid or sodium acetate solution, the arsonic acid yields a vermilion-colored precipitate which contains no arsenic and is insoluble in soda or alkali solution. Diazosulfanilic acid also readily replaces the arsonic acid residue at ordinary temperature.[1205]

5-Amino-2-methoxy-4-hydroxyphenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{array}{l} / OCH_3 \\ — NH_2 \\ \backslash OH \end{array},$$

obtained by reducing the corresponding nitro compound with sodium hydrosulfite in alkaline solution, forms aggregates of needles containing $2H_2O$. It is sparingly soluble in water, glacial acetic acid, methyl or ethyl alcohol; darkens at 120°, and is completely decomposed at higher temperatures without melting. Its yellow diazo compound couples red with resorcin. The arsonic acid produces a red-brown solution with ammoniacal silver nitrate in the cold, but on warming reduction to metallic silver occurs.[625]

5-Amino-3,4-dimethoxyphenylarsonic acid, $H_2O_3AsC_6H_2\begin{array}{l} // (OCH_3)_2 \\ \backslash NH_2 \end{array}$,

is prepared by reducing the corresponding nitro derivative with ferrous hydroxide in alkaline solution. It forms radiating clusters of needles melting with decomposition at 173°, readily soluble in dilute mineral acids or hot water but sparingly in cold water or alcohol. The hydrochloric acid solution gives a bright red coloration with a trace of potassium bichromate, and a deep red coloration on treating with nitrous acid and adding sodium β-naphthoxide. The aqueous solution develops a reddish-brown color with ferric chloride, while the ammoniacal solution gives a heavy, crystalline precipitate with calcium chloride. On reducing the arsonic acid with hypophosphorous acid a black, unidentified substance containing 93 per cent of arsenic is obtained.[1206]

4-Acetylamino-3-methoxyphenylarsonic acid,

$$H_2O_3AsC_6H_3\begin{array}{l} / OCH_3 \\ \backslash NHOCCH_3 \end{array},$$

is made by treating an alkaline solution of 4-amino-3-methoxyphenylarsonic acid with acetic anhydride at 20°. It exists as white, felt-like

needles soluble in warm water with an acid reaction and in hot N-hydrochloric acid. The substance carbonizes and decomposes at 285-7° with an evolution of gas.[1207]

3-Acetylamino-4-methoxyphenylarsonic acid results upon treating an alkaline solution of 3-acetylamino-4-hydroxyphenylarsonic acid with dimethyl sulfate at 20-30°.[643]

4-Dimethylamino-3-methoxyphenylarsonic acid,

$$\mathrm{H_2O_3AsC_6H_3}\begin{array}{l}\diagup\ \mathrm{OCH_3}\\ \\ \diagdown\ \mathrm{N(CH_3)_2}\end{array},$$

is produced by the oxidation of the corresponding arsineoxide with hydrogen peroxide in alkaline solution, and is isolated either through the lead salt, or by acidifying with hydrochloric acid, evaporating to dryness and extracting with absolute alcohol. It crystallizes in leaflets decomposing at 160°.[1208]

2-Nitro-4-amino-3-hydroxyphenylarsonic acid, $\mathrm{H_2O_3AsC_6H_2}\begin{array}{l}\diagup\ \mathrm{NO_2}\\ \text{—}\ \mathrm{NH_2},\\ \diagdown\ \mathrm{OH}\end{array}$

formed upon warming the corresponding acetylamino derivative with aqueous caustic potash on a water-bath for one and one-half hours, consists of brown-red needles very easily soluble in hot water, difficultly so in methyl alcohol, very difficultly in ethyl alcohol, and gradually blackening but not melting below 280°. Its intensely yellow diazo compound gives a luminous blue-red coloration with an alkaline solution of resorcin and a blue-violet color with R-salt. When boiled with 2N-sulfuric acid the arsonic acid yields 2,6-nitroaminophenol, while on reduction with ferrous hydroxide a very easily soluble diamino hydroxy acid results.[1209]

5-Sulfo-3-amino-4-hydroxyphenylarsonic acid, $\mathrm{H_2O_3AsC_6H_2}\begin{array}{l}\diagup\ \mathrm{NH_2}\\ \text{—}\ \mathrm{OH}\\ \diagdown\ \mathrm{SO_3H}\end{array}$,

is obtained from the corresponding arsenious acid by oxidation with 3 per cent hydrogen peroxide at 40°. The compound decomposes at 258°, and dissolves in four times its weight of boiling water. With nitrous acid it gives a deep yellow diazo solution which couples with alkaline β-naphthol to form a deep reddish-brown soluble dye. It instantly reduces ammoniacal silver nitrate, while its ammoniacal solution yields precipitates with calcium, magnesium and barium salts. On

reduction with sulfur dioxide in the presence of hydriodic acid it is converted into the corresponding arsenious acid.[651]

2-Nitro-4-acetylamino-3-hydroxyphenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{array}{l} \diagup NO_2 \\ -OH \\ \diagdown NH.COCH_3 \end{array},$$

is prepared by nitrating the corresponding acetylamino hydroxy arsonic acid at 5-10°, and crystallizes from boiling water as hard, lustrous, orange-colored needles easily soluble in methyl alcohol or hot water. Boiling with 2N-sulfuric acid converts it into 2-nitro-6-aminophenol, but with dilute caustic potash only the acetyl group is split off. The compound has no definite melting point; it begins to darken above 200°, and melts with frothing at 220°.[1195]

2-Nitro-4-amino-3-methoxyphenylarsonic acid (β), and its isomer *6-nitro-4-amino-3-methoxyphenylarsonic acid* (α),

$$H_2O_3AsC_6H_2\begin{array}{l} \diagup NO_2 \\ -OCH_3, \\ \diagdown NH_2 \end{array}$$

are simultaneously formed when the nitration product of 4-acetylamino-3-methoxyphenylarsonic acid is hydrolyzed by warming with aqueous caustic potash on a water-bath. To separate the isomers the solution is cooled to 40°, and treated with just enough sulfuric acid to turn congo paper brown, the α-isomer precipitating at once. The β-compound is obtained by adding more sulfuric acid to the filtrate until the solution imparts a blue color to congo paper, and allowing the liquid to stand for about 12 hours.

The α-derivative consists of orange-colored needles soluble in 2N-soda, N-caustic soda or sodium acetate solution with an intense orange-yellow color (distinction from its isomer). It is also soluble in warm glacial or 50 per cent acetic acid, hot N-hydrochloric acid and in 150 volumes of boiling water, but is difficultly soluble in methyl or ethyl alcohol, cold glacial or 50 per cent acetic acid and in cold N-hydrochloric acid. Its intensely lemon-yellow diazo compound couples red-violet with R-salt and yellowish-red with resorcin.

The β-compound is a bright orange-yellow substance resembling the α-isomer, but is much more soluble. It may be recrystallized from 30-40 volumes of water, and is soluble in N-hydrochloric acid, sodium acetate, carbonate or hydroxide solution with a bright yellow color,

difficultly soluble in cold but easily in hot acetic acid, methyl or ethyl alcohol. Its orange-colored diazo compound slowly couples with R-salt to a blue-violet and with resorcin to a bluish-red coloration. The above orange-colored diazo compound is identical with that obtained from 2-nitro-4-amino-3-hydroxyphenylarsonic acid, and behaves like the latter in all reactions, forming the same azo dyes.[1210]

2-Nitro-4-acetylamino-3-methoxyphenylarsonic acid (*b*) and its isomer *6-nitro-4-acetylamino-3-methoxyphenylarsonic acid* (*a*),

$$H_2O_3AsC_6H_2\begin{array}{l} \diagup NO_2 \\ -OCH_3 \\ \diagdown NHCOCH_3 \end{array} ,$$

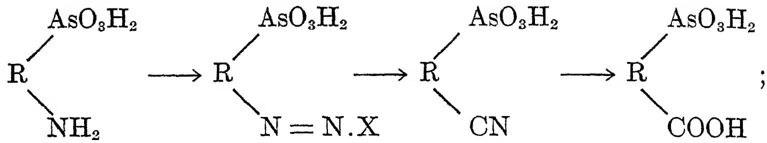
are simultaneously obtained on treating a solution of 4-acetylamino-3-methoxyphenylarsonic acid in concentrated sulfuric acid with a nitrating mixture at 5°. To separate the isomers, the product is recrystallized from boiling water, compound (b) remaining in solution. The a-isomer forms small, yellow needles soluble in water or methyl alcohol but difficultly in ethyl alcohol or cold N-hydrochloric acid. On warming its alkaline solution saponification occurs, while warm N-hydrochloric acid dissolves it with partial hydrolysis. On boiling with caustic potash, no ammonia is given off.[1210]

18. *Carboxy Aryl Arsonic Acids.*—The arsenic of aromatic organic arsenicals is so firmly attached to the nuclear carbon, that any alkyl groups present in the nucleus may be oxidized to carboxyls by means of potassium permanganate without affecting the C-As linkage. This reaction has thus far been found impossible of application with compounds of the aliphatic series; dimethylarsonic acid, for instance, is unaffected by the above reagent, while diethylarsonic acid decomposes into arsenic- and acetic acids. The most convenient method of preparing carboxy arsonic acids consists in oxidizing the homologues of phenylarsonic acid with potassium permanganate in alkaline solution, e. g.,

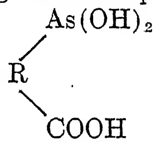
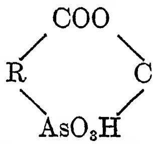
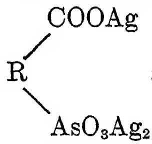
$$K_2O_3AsC_6H_3.CH_3 + K_2Mn_2O_8 \longrightarrow$$
$$K_2O_3AsC_6H_4.COOK + 2MnO_2 + KOH + H_2O.$$

In some cases prolonged heating with concentrated nitric acid in a sealed tube gives the same results. If, however, the parent substance contains an amino group, the latter must be first protected by acylating before oxidizing the alkyl group.

The carboxylic acid derivatives may also be prepared from amino arsonic acids by diazotizing, converting into nitriles and finally hydrolyzing with alkali:



or from amino carboxylic acids by Bart's reaction. In one case, a carboxy arsonic acid has been obtained from a halogenated carboxylic acid by refluxing with potassium arsenite, alcohol and metallic copper.

The members of this group are crystalline compounds soluble in water, glacial acetic acid, methyl or ethyl alcohol. They are reduced by hydriodic acid and red phosphorus to the corresponding diiodoarsines, which in turn react with sodium carbonate, yielding the corresponding carboxy aryl dihydroxyarsines or arsenious acids, . The above arsonic acids generally form salts of the type  with bivalent elements like calcium, while with univalent elements, e. g., silver, compounds corresponding to the formula  are obtained. Esters of the type $H_2O_3As.R.COOR'$ have been prepared from the corresponding arsineoxides by oxidation with hydrogen peroxide in alkaline solution. They are all crystalline solids soluble in alkalis or alcohol. The methyl ester of 4-carboxyphenylarsonic acid, however, has been derived from the trisilver salt by treating with methyl iodide.

Arsonic acids containing the group —CONHR (where R = a radical like CH_2COOH), as well as those containing the grouping —COR′ (where R′ = an aryl radical) have been obtained by oxidizing the corresponding arsineoxides with hydrogen peroxide in the usual manner. Both series of compounds consist of crystalline solids; those of the first are soluble in water or alcohol, while those of the second dissolve in hot water, alcohol or glacial acetic acid.

2-Carboxyphenylarsonic acid (*o-Benzarsonic acid*),

$H_2O_3AsC_6H_4COOH$,

may be prepared either from 2-aminobenzoic acid by Bart's method;[86] from 2-methylphenylarsonic acid by heating with nitric acid (d, 1.12)

for 12 hours in a sealed tube at 150°;[1211] or by refluxing a caustic potash solution of 2-bromobenzoic acid with aqueous potassium arsenite, alcohol and metallic copper at 90° for about 10-12 hours.[1212] It crystallizes from water in fine white needles soluble in methyl alcohol, and is distinguished from the p-isomer by the solubility of its aniline salt in water. On reduction with red phosphorus and concentrated hydriodic acid 2-carboxyphenyldiiodoarsine is formed, but with sodium hydrosulfite the product obtained is the corresponding arseno compound.

3-Carboxyphenylarsonic acid (*m-Benzarsonic acid*), from 3-methylphenylarsonic acid by oxidation with aqueous potassium permanganate in caustic potash solution, consists of lustrous leaflets readily soluble in water or alcohol. When heated it does not melt, but at 220° is transformed into the anhydride (m-arsinoxybenzoic acid), $HOOC.C_6H_4AsO_2$, a yellowish powder which is reconverted into the acid by warming with water. The calcium salt, $C_6H_4\left\langle{}^{COO}_{AsO_3H}\right\rangle Ca$, forms small, rectangular plates readily soluble in water. The silver salt,

$$AgOOC.C_6H_4.AsO(OAg)_2,$$

is a white precipitate insoluble in water.[1213]

4-Carboxyphenylarsonic acid (*p-Benzarsonic acid*) may be obtained by oxidizing 4-methylphenylarsonic acid either with aqueous potassium permanganate in alkaline solution,[1214] or by heating with dilute nitric acid (d, 1.2) in a sealed tube for 13-14 hours at 150°,[1215] or for three hours at 170°.[106] The compound may also be derived from 4-aminobenzoic acid by Bart's method,[548] or from 4-aminophenylarsonic acid by treating its diazo solution with cuprous cyanide, and hydrolyzing the resulting 4-cyanophenylarsonic acid with potassium hydroxide.[501] The acid forms large, colorless, transparent leaflets or fine needles sparingly soluble in water, cold alcohol or hot glacial acetic acid, but readily soluble in hot alcohol and in alkali hydroxides or carbonates, forming salts with the last two reagents. The acid is very stable—it is not reduced by either zinc or aluminium in alkaline solution, and when heated with dry bromine in a sealed tube at 100° yields the corresponding dibromo arsonic acid, the arsenic being split off only upon heating the acid with bromine water at 150°. When heated alone it loses one molecule of water, forming an anhydride, $C_6H_4\left\langle{}^{COOH}_{AsO_2}\right.$, a pale yellow

powder crystallizing from boiling alcohol in ill-defined crusts and decomposing at 230°.

Salts.—The acid potassium salt,

$$HOOC.C_6H_4AsO_3H_2.KOOC.C_6H_4AsO_3H_2,$$

consists of triclinic plates soluble in warm water and insoluble in absolute alcohol. Its aqueous solution has an acid reaction and liberates carbon dioxide from alkali carbonates. Fused with caustic potash, it yields phenol, while with phosphorus pentachloride it gives a chlorinated product which is converted into benzarsonic acid upon the addition of water. The potassium is removed with difficulty on dissolving the salt in dilute hydrochloric acid, and evaporating to dryness on a water bath. The calcium salt, $C_6H_4\begin{smallmatrix} / & COO & \backslash \\ \backslash & AsO_3H & / \end{smallmatrix}Ca + H_2O$, consists of nacreous leaflets sparingly soluble in cold water and more readily in hot, while the silver salt, $C_6H_4\begin{smallmatrix} / COOAg \\ \backslash AsO(OAg)_2 \end{smallmatrix}$, is a white, amorphous precipitate insoluble in water but readily soluble in ammonia or nitric acid.[1216]

Esters.—The methyl ester, $C_6H_4\begin{smallmatrix} / COOCH_3 \\ \backslash AsO(OH)_2 \end{smallmatrix}$, is derived from silver benzarsonate by heating with methyl iodide in a sealed tube at 110°. It consists of colorless, crystalline crusts which dissolve in alcohol, are insoluble in ether, do not melt on heating, and may be hydrolyzed by boiling with water but more readily with alkalis.[1217] The ethyl ester, made by oxidizing the corresponding arsineoxide with hydrogen peroxide in alkaline solution, crystallizes in small, lustrous plates soluble in aqueous sodium carbonate, and melting at about 260° with the immediate formation of an infusible powder.[1218] The cholesterin ester, $H_2O_3AsC_6H_4COOC_{27}H_{45}$, as well as its potassium salt, consists of needles difficultly soluble in alcohol. The myricyl ester, $H_2O_3AsC_6H_4COOC_{30}H_{61}$, results upon oxidation of the corresponding arsineoxide with hydrogen peroxide in acetone solution, forming minute leaflets sparingly soluble in alcohol.[106] The guaiacol ester, $H_2O_3AsC_6H_4COOC_6H_4OCH_3$, similarly prepared, exists as thin, shiny, odorless needles very soluble in aqueous sodium carbonate, soluble in alcohol or hot acetone, insoluble in ether, and decomposing without melting at a very high temperature.[546]

The quinine ester, $H_2O_3AsC_6H_4COOC_{20}H_{23}N_2O$, is obtained by first boiling together chloroform solutions of 4-dichloroarsinobenzoyl chloride and anhydrous quinine, and then oxidizing the resulting dichloroarsinobenzoylquinine hydrochloride with hydrogen peroxide. The compound crystallizes from 50 per cent alcohol in small, brilliant cubical crystals, m. p. about 200°; easily soluble in dilute mineral acids, aqueous caustic soda, sodium carbonate or ammonia but slightly in water, alcohol or acetone.[1218]

4 or 2-Carboxy-2 or 4-methylphenylarsonic acid (*m-Toluarsonic acid*), $H_2O_3AsC_6H_3\begin{array}{l}\diagup COOH\\ \diagdown CH_3\end{array}$, is made by oxidizing 2,4-dimethylphenylarsonic acid with the calculated amount of potassium permanganate. At 190° it loses one molecule of water, forming the anhydride, while above 300° it decomposes without melting. The acid is soluble in water, alcohol or ether, and forms a silver salt,

$$(HOOC)(CH_3)C_6H_3AsO(OAg)_2.$$[1219]

2-Carboxy-5-methylphenylarsonic acid (*p-Toluarsonic acid*) is prepared like the meta isomer from 2,5-dimethylphenylarsonic acid, forming white crystals, m. p. 208°; easily soluble in alcohol or ether but difficultly in water. It forms a white, amorphous silver salt.[458]

2,4-Dicarboxyphenylarsonic acid (*Isophthaloarsonic acid*),

$$H_2O_3AsC_6H_3(COOH)_2,$$

from 2,4-dimethylphenylarsonic acid by oxidation with the calculated amount of potassium permanganate in alkaline solution, consists of colorless crystals decomposing without melting when heated.[1219]

4-Nitro-2-carboxyphenylarsonic acid, $H_2O_3AsC_6H_3\begin{array}{l}\diagup NO_2\\ \diagdown COOH\end{array}$, is obtained as splendid white husks and needles on treating 5-nitroanthranilic acid according to Bart's method. With sodium hydrosulfite the compound does not yield the arseno derivative but an easily soluble sulfaminic acid.[1220]

3-Nitro-4-carboxyphenylarsonic acid is derived from 3-nitro-4-methylphenylarsonic acid by oxidation with potassium permanganate in alkaline solution at 60-70°. It crystallizes in fine, white needles

easily soluble in water or alcohol, insoluble in ether or chloroform, and remaining unmelted below 300°.[976]

4-Amino-2-carboxyphenylarsonic acid, $H_2O_3AsC_6H_3\begin{matrix}\diagup NH_2\\ \diagdown COOH\end{matrix}$, results either upon refluxing the corresponding acetylamino derivative with methyl alcoholic potash,[1221] or upon reducing the 4-nitro-2-carboxy derivative with ferrous sulfate in alkaline solution.[1222] It separates as leaflets having the same properties as the succeeding isomer.

4-Amino-3-carboxyphenylarsonic acid (*Anthranilarsonic acid*) is produced by hydrolyzing the corresponding acetylamino derivative in either acid or alkaline medium. It crystallizes from water or glacial acetic acid in needles melting with decomposition at 245°, soluble in methyl or ethyl alcohol, hot water or hot glacial acetic acid and sparingly in excess of cold hydrochloric acid, acetone or other organic solvents. The compound is a moderately strong acid. Its aqueous solution gives a reddish-yellow color with ferric chloride, but towards alkalis, magnesia mixture, calcium chloride or silver nitrate it behaves like its acetyl derivative. It can be very readily diazotized, the resulting diazo solution exhibiting the usual diazo characteristics, and coupling with amines or phenols to arsenical azo dyes.[1223]

4-Acetylamino-2-carboxyphenylarsonic acid,

$$H_2O_3AsC_6H_3\begin{matrix}\diagup COOH\\ \diagdown NH.COCH_3\end{matrix},$$

from 4-acetylamino-2-methylphenylarsonic acid by oxidizing with potassium permanganate in alkaline solution, crystallizes from water as short needles melting at 260° with decomposition. It behaves like its 3-carboxy isomer except that it is much more sensitive to the action of strong acids, so that it cannot be hydrolyzed to the corresponding amino compound by such reagents.[1224]

4-Acetylamino-3-carboxyphenylarsonic acid, prepared like the preceding compound from the 4-acetylamino-3-methylphenyl derivative at 80-95°,[1225] crystallizes from water in long, thin, hair-like crystals containing one molecule of the solvent, and from glacial acetic acid as short, felted needles melting at 230° with decomposition. It is soluble in hot water, cold methyl or ethyl alcohol, acetone, glacial acetic acid, alkali hydroxides or carbonates and very sparingly so in dilute hydro-

chloric acid or the other usual solvents. The compound is a moderately strong acid; from its solution in alkalis, alcohol precipitates the alkaline salts as white solids extremely soluble in water. It also forms calcium, magnesium and silver salts. The acetyl group may be readily split off by means of sodium hydroxide in the usual manner.

4-Acetylamino-5-carboxy-2-methylphenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{cases} CH_3 \\ COOH \\ NH.COCH_3 \end{cases},$$

is obtained from 4-acetylamino-2,5-dimethylphenylarsonic acid by oxidation with potassium permanganate in alkaline solution. It decomposes at 255°.[1226]

4-Acetylamino-2,5-dicarboxyphenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{cases} (COOH)_2 \\ NH.COCH_3 \end{cases},$$

is formed on further oxidizing the preceding compound with alkaline permanganate solution. It turns brown and decomposes at 340°.[1226]

4-Carbamido-3-carboxyphenylarsonic acid,

$$H_2O_3AsC_6H_3\begin{cases} COOH \\ NH.CONH_2 \end{cases}.$$

Aqueous disodium 4-amino-3-carboxyphenylarsonate is treated with four moles of potassium cyanate and four moles of glacial acetic acid, allowed to stand for 24 hours, and the carbamino compound precipitated with hydrochloric acid.[962]

4-Hydroxy-2-carboxyphenylarsonic acid, $H_2O_3AsC_6H_3\begin{cases} OH \\ COOH \end{cases}$, is made by oxidizing an aqueous suspension of 2,2-dicarboxy-4,4-dihydroxyarsenobenzene with 30 per cent hydrogen peroxide. It consists of snow-white needles easily soluble in water.[1222]

4-Hydroxy-3-carboxyphenylarsonic acid (*Salicylarsonic acid*), is produced by diazotizing the 4-amino-3-carboxy derivative with sodium nitrite in sulfuric acid solution, and decomposing the diazo solution by means of steam. It crystallizes from water as transparent platelets which begin to decompose at 325°, are soluble in hot water, methyl or ethyl alcohol, acetone or glacial acetic acid but practically insoluble in the other usual organic solvents. Hydrochloric and sulfuric acids do not affect it in the cold, while boiling with nitric acid splits off the arsenic. Its aqueous solution turns red congo blue, yields a red solution with ferric chloride, and forms sparingly soluble silver, calcium, magnesium, barium, copper and iron salts. The alkali salts are precipitated from water by alcohol.[1227]

5-Nitro-4-hydroxy-2-carboxyphenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{matrix} \diagup COOH \\ — NO_2 \\ \diagdown OH \end{matrix} ,$$

derived from 4-hydroxy-2-carboxyphenylarsonic acid by nitrating at 0°, consists of white needles decomposing at 350-5°.[1228]

Hippuroarsonic acid, $H_2O_3AsC_6H_4.CONHCH_2COOH$, is obtained from the corresponding arsineoxide by oxidizing with hydrogen peroxide in alkaline solution, the benzarsonic acid, which is simultaneously formed, being easily removed by virtue of its insolubility in water. The hippuroarsonic acid is easily soluble in water, methyl or ethyl alcohol, almost insoluble in the fatty solvents, and gives precipitates with calcium, barium and magnesium ions. Its trisodium salt crystallizes with four molecules of water in strongly hygroscopic, colorless needles readily absorbing carbon dioxide from the air.[547]

4-Benzoylalaninearsonic acid, $H_2O_3AsC_6H_4.CONHCH\begin{matrix} \diagup CH_3 \\ \diagdown COOH \end{matrix}$, as well as the seven succeeding acids, are obtained by the oxidation of their corresponding arsineoxides with hydrogen peroxide in alkaline solution. The above compound consists of minute, cubical crystals sparingly soluble in cold water but more easily on heating. The solution of its alkali salts, when treated with calcium chloride or magnesia mixture, becomes turbid only on warming; with copper salts it gives green precipitates soluble in ammonia to a deep blue solution from which azure blue needles containing arsenic and ammonia finally separate. With salts of other heavy metals there are obtained insoluble precipitates.

4-Benzoylleucinearsonic acid,

$$H_2O_3AsC_6H_4.CONHCH\left<\begin{matrix}CH_2CH(CH_3)_2\\ COOH\end{matrix}\right. ,$$

crystallizes as minute needles sparingly soluble in hot water.

4-Benzoylaspartic acid-1-arsonic acid,

$$H_2O_3AsC_6H_4.CONHCH\left<\begin{matrix}CH_2COOH\\ COOH\end{matrix}\right. ,$$

separates as whetstone-shaped crystals, frequently combined into husks, which are fairly soluble in cold water with an acid reaction.

4-Benzoylglutamic acid-1-arsonic acid,

$$H_2O_3AsC_6H_4.CONHCH\left<\begin{matrix}CH_2.CH_2COOH\\ COOH\end{matrix}\right. ,$$

consists in part of small cubical crystals, but for the most part it is a syrupy mass soluble in water in all proportions with an acid reaction.

4-Benzoylphenylalaninearsonic acid,

$$H_2O_3AsC_6H_4CONHCH\left<\begin{matrix}CH_2C_6H_5\\ COOH\end{matrix}\right. ,$$

exists as small needles soluble in alcohol or hot water, but otherwise resembling the alanine derivative.

4-Benzoyltyrosinearsonic acid, $H_2O_3AsC_6H_4CONHCH\left<\begin{matrix}CH_2C_6H_4OH\\ COOH\end{matrix}\right.$.

—Leaflets soluble in water or alcohol.[106]

Benzophenone-4-arsonic acid, $H_2O_3AsC_6H_4.COC_6H_5$, crystallizes from boiling water as lustrous clusters of elongated plates softening at 195° but not melting below 260°. It is soluble in alkalis, alcohol or warm glacial acetic acid but insoluble in cold water, benzene or ether.

Its oxime, $H_2O_3AsC_6H_4.C\begin{array}{l}\diagup NOH\\ \diagdown C_6H_5\end{array}$, is obtained by warming the acid with hydroxylamine sulfate in a slightly alkaline alcoholic solution, and crystallizes from hot water as fine, colorless needles which do not melt below 260°.[549]

4'-Methylbenzophenone-4-arsonic acid, $H_2O_3AsC_6H_4.COC_6H_4(CH_3)$.—Transparent plates from hot water which do not melt below 260°, are easily soluble in alkalis, somewhat soluble in ethyl alcohol and insoluble in ether, benzene, etc.[549]

3'-Nitrobenzophenone-4-arsonic acid, $H_2O_3AsC_6H_4.C\begin{array}{l}\diagup O\\ \diagdown C_6H_4.NO_2\end{array}$, consists of fine, light yellow needles obtained by treating benzophenone-arsonic acid with fuming nitric acid, and warming on a water-bath.[549]

4'-Methoxybenzophenone-4-arsonic acid,

$$H_2O_3AsC_6H_4.C\begin{array}{l}\diagup O\\ \diagdown C_6H_4.OCH_3\end{array},$$

is prepared by condensing a carbon bisulfide solution of 4-dichloro-arsinobenzoyl chloride with anisole in the presence of aluminium chloride, converting the product into the arsineoxide by means of sodium carbonate, and oxidizing this oxide, without attempting to isolate it, by means of hydrogen peroxide. It may be recrystallized from hot water.[1229]

4'-Ethoxybenzophenone-4-arsonic acid, prepared in a similar manner from phenetole, may be recrystallized only from glacial acetic acid or 95 per cent ethyl alcohol, as water dissolves the compound with great difficulty.[1229]

4'-Phenoxybenzophenone-4-arsonic acid is produced in the same way using diphenyl ether. It crystallizes from hot glacial acetic acid or 95 per cent alcohol as colorless platelets which do not melt below 260°, and are practically insoluble in boiling water.[1229]

19. *Aryl Arsonic Acids Containing Mercury.*—The introduction of mercury into the nuclei of aryl arsonic acids has been found possible

by the interaction of solutions of the above acids or their sodium salts and mercuric acetate, forming acetoxymercuriarsonic acids of the general formula $R\begin{array}{l} \diagup HgOOCH_3 \\ \diagdown AsO(OH)_2 \end{array}$. These in turn yield, on subsequent treatment with dilute alkalis, the corresponding hydroxymercuri derivatives of the formula $R\begin{array}{l} \diagup HgOH \\ \diagdown AsO(OH)_2 \end{array}$, which react with still more alkali, forming salts. The free acids are generally insoluble in water or the usual organic solvents, soluble in alkalis and, in many cases, in glacial acetic or 10 per cent hydrochloric acid. The alkaline solutions, on prolonged exposure to air, gradually decompose, free mercury being deposited.

3-Hydroxymercuri-4-aminophenylarsonic acid, $H_2O_3AsC_6H_3\begin{array}{l} \diagup HgOH \\ \diagdown NH_2 \end{array}$,

and *3,5-dihydroxymercuri-4-aminophenylarsonic acid,*

$$H_2O_3AsC_6H_2\begin{array}{l} /\!\!/ (HgOH)_2 \\ \diagdown NH_2 \end{array};$$

are simultaneously formed upon allowing sodium-p-arsanilate and mercuric acetate to interact in water at 100° for five hours. They are isolated through their disodium salts which are separated by fractional crystallization. The monohydroxymercuri compound forms small tabular crystals insoluble in water or the usual organic solvents, while the dihydroxymercuri derivative separates as small plates. Their disodium salts crystallize with $4H_2O$ in the form of small, glistening needles readily soluble in hot water but sparingly in cold.[1230]

5-Hydroxymercuri-4-amino-3-methylphenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{array}{l} \diagup CH_3 \\ - NH_2 \\ \diagdown HgOH \end{array},$$

is a crystalline solid soluble in alkalis, forming mono- and di-metallic salts.[1230]

5-Acetoxymercuri-3-bromo-4-aminophenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{array}{l}\diagup Br\\ -NH_2\\ \diagdown HgOOCH_3\end{array},$$

is a white powder soluble in dilute sodium hydroxide, 10 per cent hydrochloric or warm glacial acetic acid.[1231]

5-Acetoxymercuri-3-bromo-4-oxalylaminophenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{array}{l}\diagup Br\\ -NH.COCOOH.\\ \diagdown HgOOCCH_3\end{array}$$

A white powder soluble in very dilute caustic soda, from which solution metallic mercury is deposited on standing.[1231]

5-Acetoxymercuri-3-nitro-4-aminophenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{array}{l}\diagup NO_2\\ -NH_2\\ \diagdown HgOOCCH_3\end{array},$$

consists of a bright yellow powder soluble in warm, very dilute sodium hydroxide, 10 per cent hydrochloric acid, glacial or warm 15 per cent acetic acid but slightly soluble in methyl alcohol.[1232]

3,5-Dihydroxymercuri-4-hydroxyphenylarsonic acid,

$$H_2O_3AsC_6H_2\begin{array}{l}/\!\!/ (HgOH)_2\\ \diagdown OH\end{array},$$

is obtained as a crystalline solid soluble in dilute alkali, forming a water-soluble trisodium salt. When an aqueous solution of this salt is treated with sodium chloride and acidified with hydrochloric acid, a white crystalline *dichloromercuri derivative,* $H_2O_3AsC_6H_2\begin{array}{l}/\!\!/ (HgCl)_2\\ \diagdown OH\end{array}$, results.[1230]

5-Hydroxymercuri-4-hydroxy-3-methylphenylarsonic acid,

$$H_2O_3AsC_6H_2 \begin{array}{l} \diagup HgOH \\ — OH \\ \diagdown CH_3 \end{array} ,$$

also forms crystals which dissolve in dilute alkali to yield a water-soluble trisodium salt.[1230]

5-Acetoxymercuri-3-nitro-4-hydroxyphenylarsonic acid,

$$H_2O_3AsC_6H_2 \begin{array}{l} \diagup NO_2 \\ — OH \\ \diagdown HgOOCCH_3 \end{array} ,$$

is a yellow powder soluble in dilute sodium hydroxide solution.[1233]

2-Acetoxymercuri-3,5-dinitro-4-hydroxyphenylarsonic acid,

$$H_2O_3AsC_6H \begin{array}{l} /\!\!/ (NO_2)_2 \\ — OH \\ \diagdown HgOOCCH_3 \end{array} .$$

A pale yellow powder only partially soluble in dilute caustic soda, a pale yellow turbidity persisting.[1234]

2 or 6-Acetoxymercuri-3-amino-4-hydroxyphenylarsonic acid,

$$H_2O_3AsC_6H_2 \begin{array}{l} \diagup NH_2 \\ — OH \\ \diagdown HgOOCCH_3 \end{array} ,$$

consists of a brown powder soluble in dilute caustic soda, from which solution metallic mercury is soon precipitated. It is also slightly soluble in cold glacial acetic or 10 per cent hydrochloric acids.[1234]

2-Acetoxymercuri-3,5-diamino-4-hydroxyphenylarsonic acid,

$$H_2O_3AsC_6H \begin{array}{l} /\!\!/ (NH_2)_2 \\ — OH \\ \diagdown HgOOCCH_3 \end{array} ,$$

separates as a dark brown powder soluble in very dilute sodium hydroxide, from which solution metallic mercury is deposited on standing.

It is also soluble in 10 per cent hydrochloric acid and partially in gl
acetic acid.[1235]

2-Acetoxymercuri-3,5-di(acetylamino)-4-hydroxyphenylarsonic

$$H_2O_3AsC_6H \begin{cases} (NH.COCH_3)_2 \\ —OH \\ HgOOCCH_3 \end{cases} ,$$

is a gray prowder partially soluble in cold glacial acetic acid and so
in dilute sodium hydroxide, from which solution metallic mercury
cipitates on standing.[1236]

2-Acetoxymercuri-4-carboxyphenylarsonic acid,

$$H_2O_3AsC_6H_3 \begin{cases} HgOOCCH_3 \\ COOH \end{cases} ,$$

is a cream-colored powder soluble in concentrated aqueous so
chloride, dilute hydrochloric or warm glacial acetic acid. Aqu
sodium hydroxide does not dissolve it, but forms a yellow precipitat

3,5-Dihydroxymercuri-4-hydroxy-1′-methylazobenzene-4′-ar
acid, $H_2O_3AsC_6H_3 \begin{cases} CH_3 \\ N{:}N.C_6H_2 \begin{cases} (HgOH)_2 \\ OH \end{cases} \end{cases}$, consists of a sc
amorphous solid soluble in aqueous caustic soda, forming a water-so
trisodium salt.[1230]

5,5′-Mercuri-bis(3-nitro-4-hydroxyphenylarsonic acid),

$$\begin{array}{ccc} H_2O_3As & & AsO_3H_2 \\ O_2N—C_6H_2 & .Hg. & C_6H_2—NO_2 \\ HO & & OH \end{array} ,$$

is produced by warming an alkaline solution of 5-acetoxymercu
nitro-4-hydroxyphenylarsonic acid with successive portions of aqu
sodium hydrosulfide until the filtrate gives a negative test with so
stannite. The free acid, isolated by treating a hot solution o
ammonium salt with an excess of dilute sulfuric acid, is a very hy

scopic yellow powder insoluble in all organic solvents, and is unaffected by sodium stannite in alkaline solution. Like other compounds of this type it has no melting point.[1238]

20. *Aryl Trithioarsonic Acids and Arsinedisulfides.*—$RAsS(SH)_2$ and $RAsS_2$. On passing hydrogen sulfide through ammoniacal solutions of various arsonic acids, there are formed ammonium salts of the corresponding trithioarsonic acids, which upon treatment with hydrochloric acid yield the free thio acids:

$$RAsO(ONH_4)_2 \longrightarrow RAsS(SNH_4)_2 \longrightarrow RAsS(SH)_2.$$

The latter, however are so unstable that they decompose according to either one of the two following equations, depending upon the working conditions and the nature of the nuclear substituents:

$$RAsS(SH)_2 \longrightarrow RAsS_2 + H_2S$$
$$2RAsS(SH)_2 \longrightarrow R_2As_2S_3 + 2H_2S + S.$$

On the other hand, the alkali salts of trithioarsonic acids are very stable, and can be prepared from arylarsinesulfides or -sesquisulfides by treatment with alkali sulfides and sulfur, or with alkali polysulfides:

$$RAsS + \underbrace{Na_2S + S}_{Na_2S_2} \longrightarrow RAsS_3Na_2$$

$$R_2As_2S_3 + 2Na_2S + S \longrightarrow 2RAsS_3Na_2.$$

It is interesting to note that the free 3-amino-4-methylphenyltrithioarsonic acid has been obtained as a sulfate by reducing the corresponding nitro arsonic acid with hydrogen sulfide.

The disulfides are formed by the action of hydrogen sulfide upon arsonic acids:

$$RAsO_3H_2 + 2H_2S \longrightarrow RAsS_2 + 3H_2O;$$

by the decomposition of trithioarsonic acids; or upon the addition of sulfur to arseno compounds:

$$RAs = AsR + 2S_2 \longrightarrow 2RAsS_2.$$

Disodium phenyltrithioarsonate, $C_6H_5AsS\begin{cases} SNa \\ SNa \end{cases}$, is obtained by treating phenylarsinesulfide or -sesquisulfide with a solution of sodium hydrosulfide containing sulfur. It forms fine needles easily soluble in water but difficultly in alcohol.[1239]

3-Amino-4-methylphenyltrithioarsonic acid, $H_2S_3AsC_6H_3\begin{array}{l}\diagup CH_3\\ \diagdown NH_2\end{array}$, is prepared by saturating an ammoniacal solution of 3-nitro-4-methylphenylarsonic acid with hydrogen sulfide, warming on the water-bath for twelve hours, adding fresh ammonia, and again saturating with hydrogen sulfide. The compound is then isolated as the sulfate by evaporating the liquid to dryness, digesting the residue with very dilute hydrochloric acid, and treating the filtered solution with dilute sulfuric acid. The salt is a yellowish, amorphous powder which begins to decompose at 155°, does not dissolve in water or organic solvents, but is readily soluble in dilute alkalis, from which it is reprecipitated by sulfuric acid. In addition, concentrated hydrochloric acid appears to precipitate a difficultly soluble hydrochloride.[1240]

Benzylarsinedisulfide, $C_6H_5CH_2AsS_2$, slowly separates as a heavy, bright yellow oil, sparingly soluble in water, on treating an aqueous solution of benzylarsonic acid with hydrogen sulfide. It dissolves rapidly in nitric acid with liberation of sulfur and oxides of nitrogen. When heated alone, it decomposes, yielding hydrogen sulfide, arsenic trioxide and stilbene.[1241]

2,5-Dimethylphenylarsinedisulfide, $(CH_3)_2C_6H_3AsS_2$, results on saturating an ammoniacal solution of the corresponding arsonic acid with hydrogen sulfide and acidulating with hydrochloric acid. It separates as a white precipitate which may be recrystallized from benzene, and melts at 95°.[554]

3-Nitrophenylarsinedisulfide, $C_6H_4\begin{array}{l}\diagup AsS_2\\ \diagdown NO_2\end{array}$, is made by boiling an aqueous suspension of dinitroarsenobenzene with flowers of sulfur for about one hour, then rendering ammoniacal, filtering and precipitating with hydrochloric acid. It is a white powder melting at about 80° and intumescing at higher temperatures, readily soluble in ammonia or aqueous alkalis, slightly in alcohol or benzene but insoluble in water, ether or chloroform.[565]

Phenylglycine-4-arsinedisulfide, $HOOCCH_2HN.C_6H_4.AsS_2$, is a yellowish-white substances produced by saturating an aqueous solution of the corresponding arsonic acid with hydrogen sulfide. The compound is soluble in soda but difficultly so in organic solvents, with the exception

of the bases. It gradually assumes a yellow color on exposure to light, begins to sinter at 70°, and decomposes at 142°.[559]

p-(Acetylmercapto)aminophenylarsylene disulfide [*S-Acetylhydrosulfaminophenyl-4-arsinedisulfide*], $(CH_3CO.S.HN)C_6H_4AsS_2$, is prepared by introducing atoxyl into aqueous formaldehydesulfoxylate at 70°, and treating the cooled solution with thioacetic acid. After standing over night there is formed at the bottom of the vessel a yellow solid which is purified by dissolving in pyridine and reprecipitating with methyl alcohol. The red compound obtained melts with decomposition at 183°.[990]

B. Secondary Derivatives.

1. *Diaryl Arsinetrihalides and -Oxyhalides,* R_2AsX_3.—The simplest method of preparing compounds of the above type consists in treating diaryl monohalogenated arsines with anhydrous halogens:

$$R_2AsX + X_2 \longrightarrow R_2AsX_3$$

The same products may be produced by the action of halogens upon aromatic cacodyls:

$$R_2As.AsR_2 + 3X_2 \longrightarrow 2R_2AsX_3;$$

and by the interaction of diarylarsines and halogens:

$$R_2AsH + 2X_2 \longrightarrow R_2AsX_3 + HX.$$

None of these methods, however, have been employed in the preparation of dibenzylarsinetrichloride; it results upon heating tribenzylarsine with an excess of benzyl chloride in a sealed tube at 200°, and is also one of the products formed on condensing benzyl chloride with arsenic trichloride by means of sodium. The diaryl arsinetrihalides are solids generally decomposed by water, yielding the corresponding diarylarsinic acids:

$$R_2AsX_3 + 2H_2O \longrightarrow R_2AsO.OH + 3HX$$

Diaryl arsineoxides combine additively with dry halogens, forming the corresponding arsineoxyhalides, which are easily decomposed by water into diarylarsinic acids:

$$(R_2As)_2O + 2X_2 \longrightarrow (R_2AsX_2)_2O$$
$$(R_2AsX_2)_2O + 3H_2O \longrightarrow 2R_2AsO.OH + 4HX.$$

Aryl esters of the hypothetical compound $R_2As(OH)X_2$ are obtained by the action of halogens upon esters of diphenylarsenious acid in anhydrous solvents. They are crystalline substances which hydrolyze to phenol, diarylarsinic and haloid acids:

$$R_2As(OR') + X_2 \longrightarrow R_2As(OR')X_2$$
$$R_2As(OR')X_2 + 2H_2O \longrightarrow R_2AsO.OH + 2HX + R'OH.$$

A dicamphorylarsineoxychloride corresponding to the formula R_2AsOCl has been obtained by the action of phosphorus pentachloride upon dicamphorylarsinic acid:

$$R_2AsO.OH + PCl_5 \longrightarrow R_2AsOCl + POCl_3 + HCl.$$

The above compound is the only representative of this type of aromatic arsenicals.

Diphenylarsinetrichloride, $(C_6H_5)_2AsCl_3$, may be obtained either by the action of dry chlorine on diphenylchloroarsine,[1242] or by bringing chlorine in contact with phenyl cacodyl.[1243] It crystallizes from warm benzene as colorless plates, m. p. 174°; easily decomposed by water into diphenylarsinic and hydrochloric acids. When heated gently in a current of carbon dioxide it decomposes into diphenylchloroarsine and chlorine, while heating in a sealed tube at 200° yields chlorobenzene and phenyldichloroarsine.

Diphenylarsinechlorobromide, $(C_6H_5)_2AsCl.Br_2$, results upon allowing dry bromine vapors to act upon diphenylchloroarsine. It is a flesh-colored solid soluble in hot benzene or ether with partial decomposition, and fuming slightly on exposure to air.[1244]

Diphenylarsinetribromide is precipitated on allowing diphenylarsine to distil slowly into ether containing bromine. It forms golden-yellow plates, m. p. 129°; attacks the skin with great avidity, and is decomposed by water, forming diphenylbromoarsine.[1245]

Di(4-methylphenyl)arsinetrichloride, $(CH_3.C_6H_4)_2AsCl_3$, is a pale yellow, pulverulent mass obtained by the action of dry chlorine upon the corresponding chloroarsine.[1246]

Dibenzylarsinetrichloride, $(C_6H_5.CH_2)_2AsCl_3$, is prepared either by condensing benzyl chloride and arsenic trichloride by means of sodium,[826] or by heating tribenzylarsine with an excess of benzyl chloride in a sealed tube at 200°.[1247]

Di(3-nitrophenyl)arsinetrichloride, $(O_2N.C_6H_4)_2AsCl_3$, results upon treating a benzene suspension of tetra(3-nitrophenyl)diarsine with chlorine until complete solution is effected.[743]

Di(3-nitrophenyl)arsinetribromide is formed from the corresponding bromoarsine by treating with bromine in benzene, and allowing to concentrate in vacuo. It is a deliquescent solid readily converted into di(3-nitrophenyl)arsinic acid by moisture.[743]

Diphenylarsineoxychloride,
$$\begin{array}{l} \qquad\qquad\quad Cl_2 \\ (C_6H_5)_2As \diagup\!\!\!\diagup \\ \qquad\qquad\quad \diagdown \\ \qquad\qquad\qquad O \\ \qquad\qquad\quad \diagup \\ (C_6H_5)_2As \diagdown\!\!\!\diagdown \\ \qquad\qquad\quad Cl_2 \end{array}$$
, formed by the action of dry chlorine upon diphenylarsineoxide, is a white powder, m. p. 117°; soluble in hot benzene, and easily decomposed by water into diphenylarsinic and hydrochloric acids.[748]

Phenyl-p-tolylarsineoxychloride, $\left[\begin{array}{l} C_6H_5 \diagdown \\ \qquad\qquad AsCl_2 \\ CH_3.C_6H_4 \diagup \end{array}\right]_2O$, similarly prepared, consists of colorless, fan-shaped aggregates of needles.[780]

Dicamphorylarsineoxychloride, $(C_{10}H_{15}O)_2AsO.Cl$. From potassium dicamphorylarsinate and phosphorus pentachloride. It crystallizes from chloroform and benzene as colorless crystals melting at 158°, and is rapidly decomposed on exposure to atmospheric moisture.[1248]

Phenyl ester of diphenylarsinehydroxychloride,

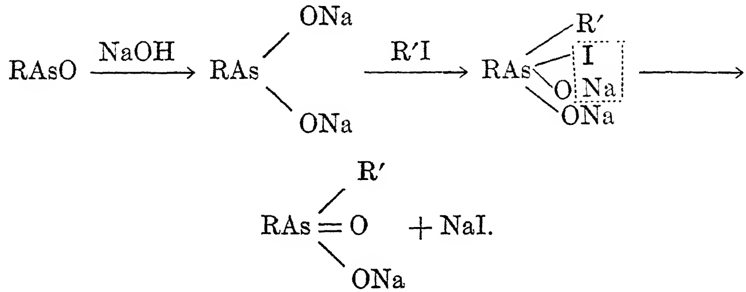
$$(C_6H_5)_2As(OC_6H_5)Cl_2,$$

results when chlorine acts upon the phenyl ester of diphenylarsenious acid in petroleum ether solution. It crystallizes in white needles, m. p. 121-2°; readily hydrolyzed by water to phenol, hydrochloric and diphenylarsinic acids.[1249]

The *phenyl ester of diphenylarsinehydroxybromide* is similarly obtained as yellowish-red crystals melting at 100°, and hydrolyzing as above.[775]

Diphenylcyanoarsinedichloride, $(C_6H_5)_2As\begin{array}{l} \diagup\!\!\!\diagup Cl_2 \\ \diagdown CN \end{array}$. On passing chlorine through a benzene solution of diphenylcyanoarsine, filtering off the solid which separates, and allowing the filtrate to stand, the above product separates out in the course of a few days as a crystalline substance melting at 130-33°. The compound is fairly stable when dry but is hydrolyzed upon boiling with water, needles of diphenylarsinic acid separating on cooling.[1250]

2. *Arsinic Acids.*—Arsinic acids in which the arsenic is attached to one aryl and one alkyl group may be prepared by a further application of Meyer's method. The procedure consists in treating an arylarsine-oxide with an alkyl iodide in the presence of alkali, the resulting reaction being represented as follows:



The unsubstituted diarylarsinic acids may be obtained:

1. From the corresponding arsinetrichlorides by treatment with water. It is not necessary to isolate the trihalide, as the arsinic acid separates directly upon treating the chloroarsine with chlorine in the presence of water, the following two reactions occurring simultaneously:

$$\left\{\begin{array}{l} R_2AsCl + Cl_2 \longrightarrow R_2AsCl_3 \\ R_2AsCl_3 + 2H_2O \longrightarrow R_2AsO.OH + 3HCl. \end{array}\right.$$

2. By hydrolyzing the corresponding arsineoxychlorides:

$$(R_2AsX_2)_2O + 3H_2O \longrightarrow 2R_2AsO.OH + 4HX.$$

3. From diaryl cyanoarsines or arsineoxides by oxidation:

$$R_2AsCN + O + H_2O \longrightarrow R_2AsO.OH + HCN$$
$$(R_2As)_2O + O + H_2O \longrightarrow 2R_2AsO.OH.$$

The unsubstituted arsinic acids which are well-defined crystalline compounds soluble in water, alcohol or acetic acid, are amphoteric, forming salts with both acids and bases. The alkali and alkali earth salts are generally hygroscopic and readily soluble in water, while those of the heavy metals are, as a rule, insoluble. The salts with acids are usually unstable and readily hydrolyzed by water. Unlike the aryl arsonic acids, the arsinic acids do not form anhydrides upon heating. When reduced with phosphorous acid they yield tetraaryldiarsines.

Many nuclear substituted arsinic acids have also been obtained, in quite a few cases by methods similar to those employed in the preparation of primary arsonic acids. They exhibit properties characteristic of both arsinic acids and the particular groups present in the ring.

Compounds of the general type $\begin{array}{l} C_6H_5 \\ HOOCCH_2 \end{array} > AsO.ONa$ or $\begin{array}{l} C_6H_5 \\ RHNOCCH_2 \end{array} > AsO.ONa$ are very easily produced from halogenated acids or -anilides and sodium arylarsenites. The latter are not actually isolated but are formed as intermediate products. The procedure consists in dissolving an aryl dichloroarsine in four moles of alkali and gradually adding one mole of the halogen compound, generally at room temperature. The reactions usually proceed rapidly enough so that neither heating nor stirring is necessary, and are completed within a very few hours. To isolate the products, which for the most part are not very soluble in water, the reaction mixture is neutralized to phenolphthalein with hydrochloric acid, causing a precipitation of any unchanged aromatic arsineoxide, and the filtrate rendered very slightly acid to congo, the desired product precipitating in almost quantitative yield. The majority of these compounds have no melting points but have decomposition points varying considerably with the speed at which the temperature of the bath is raised.

Phenylmethylarsinic acid, $\begin{array}{l} CH_3 \\ C_6H_5 \end{array} > AsO.OH$.—Phenylarsineoxide, dissolved in alcohol and caustic soda, is mixed with methyl iodide, allowed to react over night, the hydriodic acid removed by means of silver nitrate and nitric acid, and the filtrate treated successively with silver nitrate and concentrated ammonia. The silver salt of the arsinic acid then separates as a white precipitate, from which the free acid is obtained by decomposing with 2N-hydrochloric acid. It crystallizes from water upon the addition of acetone, in silky needles, m. p. 179.5°; very soluble in water, alcohol or glacial acetic acid, but difficultly in acetone or ether. Its aqueous solution is neutral to methyl orange, but can be titrated with barium hydroxide in the presence of litmus.

The compound is amphoteric, forming salts with metallic bases as well as with hydrochloric and nitric acids. The barium salt is a water-soluble, white, hygroscopic powder; the lead salt consists of a white powder easily soluble in water, while the white mercuric salt is less soluble than the silver salt.[1251]

Phenylethylarsinic acid, $\begin{array}{l} C_2H_5 \diagdown \\ \qquad AsO.OH, \\ C_6H_5 \diagup \end{array}$ may be prepared like the preceding compound through the silver salt, or by removing the hydriodic acid from the reaction mixture with freshly precipitated silver chloride, and acidifying the filtrate with hydrochloric acid. When recrystallized from ethyl acetate it separates in colorless tetrahedral prisms, m. p. 108°; very easily soluble in water, chloroform, glacial acetic acid, methyl or ethyl alcohol, less so in benzene or acetone and difficultly in ether or ligroin.[1252]

Phenylisoamylarsinic acid, $\begin{array}{l} C_5H_{11} \diagdown \\ \qquad AsO.OH, \\ C_6H_5 \diagup \end{array}$ is obtained in the same general way, forming colorless, partially star-shaped prismatic crystals which closely resemble phenylmethylarsinic acid. It melts at 108°, is easily soluble in methyl or ethyl alcohol, ether, acetone, glacial acetic acid, chloroform, ethyl acetate or benzene but difficultly in petroleum ether. When heated in water it first melts and then dissolves.[1253]

Diphenylarsinic acid, $(C_6H_5)_2AsO.OH$, is produced by the action of water upon diphenylarsineoxychloride,[1254] or by suspending diphenylchloro arsine in water, introducing chlorine at 60-70° until all is dissolved, and evaporating the solution to dryness.[786] A better yield is obtained by heating a mixture of triphenylarsine and arsenic trichloride at 220° for 30 hours, cooling, pouring into water, and saturating the solution with chlorine. From the filtered solution the arsenic- and phenylarsonic acids are removed by boiling with magnesia mixture, and the arsinic acid precipitated from the filtrate by acidifying with hydrochloric acid.[1255] The same product is derived from diphenylcyanoarsine by treating with hydrogen peroxide (2 per cent), with bromine water in the cold, or with concentrated nitric acid on a water-bath; also from the corresponding arsineoxide by oxidizing with hydrogen peroxide.[766] The compound consists of white needles, m. p. 174°; soluble in alkalis, water or alcohol and sparingly in hot ether or benzene. When heated at 190-200° it partially sublimes without forming an anhydride. It is unaffected by hot nitric or chromic acid, but forms a nitrate, $(C_6H_5)_2AsO.ONO_3$, when introduced into a mixture of fuming nitric and concentrated sulfuric acids at low temperature. This salt crystallizes from glacial acetic acid as fine white needles melting at 125°, decomposing at higher temperatures, and insoluble in the ordinary

organic solvents. On boiling in water it first melts, and then hydrolyzes to diphenylarsinic and nitric acids.

Salts.—The sodium salt is a very hygroscopic white powder; the ammonium salt is completely dissociated over sulfuric acid; the barium salt, $[(C_6H_5)_2AsO.O]_2Ba$ is a white, viscous, scarcely crystalline mass; the calcium salt forms very deliquescent fine needles; the lead and silver salts exist as lustrous needles difficultly soluble in hot water, while with copper two salts are formed—a light blue precipitate of the neutral salt, $[(C_6H_5)_2AsO.O]_2Cu$, and a basic salt.

$$(C_6H_5)_2AsO.OCu(OH).$$ [1256]

When the arsinic acid is dissolved in an excess of warm dilute hydrochloric acid there separate, on cooling, colorless, monoclinic crystals having the formula $[(C_6H_5)_2AsO.OH]_2.HCl$, m. p. 111-111.5°; soluble in chloroform and slightly so in benzene or ether. If, however, the solvent is concentrated hydrochloric acid the compound obtained melts at 134° and has the composition $(C_6H_5)_2AsO.OH.HCl$. These two compounds may be easily converted one into the other: the first into the second by dissolving in warm concentrated hydrochloric acid, and the second into the first by heating in chloroform solution with an equimolecular quantity of diphenylarsinic acid.[1257] Two similar hydrobromides, m. p. 119.5-120° and 126-126.5° respectively, have also been prepared in the same way.[1258] These four compounds are all hydrolyzed by water into their components.

Upon treating an aqueous solution of sodium diphenylarsinate with molybdic acid, and adding an excess of guanidinium chloride to the concentrated filtrate there is obtained a compound which crystallizes from water in hexagonal plates having the formula

$$(CN_3H_6)_2H\left[\begin{array}{c}(C_6H_5)_2\\ As(Mo_2O_7)_2\\ (OH)_2\end{array}\right].H_2O.$$ [1259]

Phenyl-p-tolylarsinic acid, $\begin{array}{l}C_6H_5\diagdown\\ \qquad\quad AsO.OH,\\ CH_3.C_6H_4\diagup\end{array}$ is produced like diphenylarsinic acid from pure phenyl-p-tolylchloroarsine and chlorine in aqueous medium, separating at first as an oil which, after standing for several days, solidifies to an aggregate of white needles, m. p. 158-60°. It is readily soluble in benzene, alcohol, concentrated nitric acid or hot water but very slightly in ether or cold water. It forms a white silver salt.[780]

Phenylbenzylarsinic acid, $\begin{matrix} C_6H_5 \diagdown \\ C_6H_5.CH_2 \diagup \end{matrix} AsO.OH$.—Phenylarsineoxide in alkaline alcohol is mixed with freshly distilled benzyl chloride and allowed to stand for three days, when the sodium chloride is filtered off, the solution diluted with water, and the unchanged benzyl chloride extracted with ether. Upon neutralizing with hydrochloric acid and recrystallizing from alcohol the free acid separates as pure white, shiny needles, m. p. 206-7°; easily soluble in methyl alcohol or glacial acetic acid but difficultly in water, acetone or ether. Hot concentrated hydrochloric acid splits it into benzyl chloride and phenylarsineoxide or phenyldichloroarsine.[1260]

Di(4-methylphenyl)arsinic acid, $(C_7H_7)_2AsO.OH$.—On carefully treating the corresponding arsinetrichloride with water, the above acid is obtained as a white mass crystallizing from alcohol in granular crystals, m. p. 167°; sparingly soluble in hot water or dilute hydrochloric acid. Its alkali and alkali earth salts are easily soluble in water, the former also dissolving in alcohol. The silver salt is white.[1246]

Dibenzylarsinic acid, $(C_6H_5.CH_2)_2AsO.OH$, is obtained by condensing benzyl chloride and arsenic trichloride by means of sodium in dry ether containing a little pure ethyl acetate, and treating the dibenzylarsinetrichloride thus formed with caustic alkali.[826] The acid crystallizes from alcohol in white, highly refractive, nacreous leaflets, m. p. 210°; readily soluble in hot alcohol but sparingly in ether, benzene, acetone or hot water. It has a saline, bitter taste and a very irritating effect upon the mucous membrane. Above 210° it decomposes according to the equation:

$$2(C_6H_5.CH_2)_2AsO.OH \longrightarrow$$
$$As_2 + 2H_2O + 2C_6H_5CHO + (C_6H_5.CH_2)_2;$$

warming with concentrated hydrochloric acid decomposes it completely as follows:

$$(C_6H_5.CH_2)_2AsO.OH + + 4HCl \longrightarrow$$
$$C_6H_5CH_2Cl + C_6H_5.CH_3 + AsCl_3 + 2H_2O;$$

alkaline potassium permanganate or concentrated nitric acid oxidizes it to arsenic- and benzoic acids only after prolonged boiling, while red fuming nitric acid nitrates it in the cold but decomposes it at boiling temperature. The compound may be reduced with zinc or stannous chloride and alcoholic hydrochloric acid to an unidentified white, sparingly soluble powder which regenerates the dibenzylarsinic acid on exposure to air.

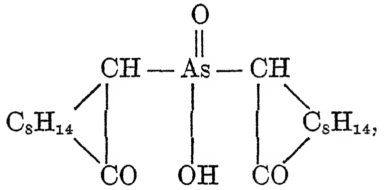
Like cacodylic acid it exhibits amphoteric properties, forming salts with both acids and bases. The hydrochloride

$$(C_6H_5.CH_2)_2AsO.OH.HCl,$$

is prepared by warming the arsinic acid with dilute hydrochloric acid, and consists of white needles melting at 128°, unstable in air, and easily hydrolyzed by water; the hydrobromide is obtained in the same way and has similiar properties, while the nitrate, consisting of silky needles melting at 128-9°, is comparatively more stable, and is hydrolyzed by water into its components. The alkali salts are well-defined, deliquescent, crystalline substances soluble in water or alcohol; the barium salt crystallizes with eight and the calcium compound with six molecules of water, while the silver salt, an amorphous precipitate sensitive to light, is soluble in dilute nitric acid, sparingly so in dilute ammonia and insoluble in water or alcohol.[1261]

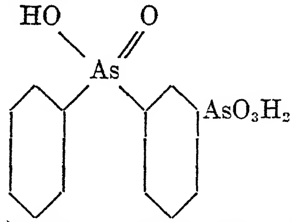
Dibenzylthioarsinic acid, $(C_6H_5.CH_2)_2AsO.SH$, results upon passing hydrogen sulfide into an alkaline solution of dibenzylarsinic acid, and neutralizing with dilute hydrochloric acid. It crystallizes from alcohol in white, nacreous leaflets melting at 197-9°.[1262]

Dicamphorylarsinic acid,



results from the interaction of sodium camphor and arsenic trichloride in toluene with the exclusion of moisture. After successive crystallizations from benzene and alcohol, it is obtained as colorless, highly refractive, obliquely truncated prisms, m. p. 266° with decomposition, soluble in benzene, chloroform or alcohol, and almost insoluble in water or petroleum. The salts of the alkali metals and ammonium are extremely soluble in water or alcohol, are stable in hot aqueous solution but hydrolyze on evaporation with an excess of caustic alkali. Both the free acid and the alkali salts decompose at 300°. The calcium, strontium, barium, nickel and cobalt salts are not precipitated in aqueous solutions, while the ferric, mercuric and cupric salts are almost insoluble in water. The silver salt is a white, sparingly soluble precipitate, amorphous at first but gradually becoming crystalline, especially on warming. The cadmium salt is a sparingly soluble white crystalline compound. The free acid is liberated from aqueous solutions of its salts by acetic acid, but only to a very slight extent by carbonic acid.[1263]

Diphenylarsinic acid-2-arsonic acid,



is derived either from 2-aminodiphenylarsinic acid by diazotizing and coupling with alkaline sodium arsenite,[1264] or by mixing an ice-cold alkaline solution of phenyldichloroarsine with o-diazophenylarsonic acid, allowing to react for 12 hours, and neutralizing the filtrate with fuming hydrochloric acid. The admixture of o-azobenzenediarsonic acid is largely removed by dissolving the product in hot sodium carbonate solution, and precipitating with hot acetic acid. The last traces of impurity are removed from the filtrate by carefully adding hot hydrochloric acid until a turbidity forms, treating with charcoal and filtering. The pure compound is then obtained by acidifying the filtrate. Upon neutralizing its hot dilute alkaline solution with hydrochloric acid it separates as microscopic, tetragonal leaflets darkening and melting at 350° with evolution of gas, and very difficultly soluble in water, acetic acid or the usual organic solvents. It yields a precipitate on boiling with magnesia mixture, and forms insoluble barium and copper salts.[1265]

2-Nitrodiphenylarsinic acid, $(C_6H_5)(O_2N.C_6H_4)AsO.OH$, crystallizes from hot alcohol in yellow needles, and from hot water in pale yellow rhombohedra, m. p. 197-8°; easily soluble in glacial acetic acid or hot alcohol, less so in hot water and almost insoluble in ether, benzene or cold water. It results upon mixing a diazo solution of 2-nitroaniline with an alkaline solution of phenyldichloroarsine at low temperature, and subsequently neutralizing with dilute hydrochloric acid.[953]

3′-Nitrodiphenylarsinic acid-2-arsonic acid, $(H_2O_3AsC_6H_4)(O_2N.C_6H_4)AsO.OH$, consists of colorless crystals which dissolve in alkalis to a yellow solution. It is prepared by nitrating diphenylarsinic acid-2-arsonic acid with a mixture of fuming nitric and sulfuric acids at 20°.[1266]

Di(3-nitrophenyl)arsinic acid, $(O_2N.C_6H_4)_2AsO.OH$, prepared by nitrating the corresponding arsinic acid,[1267] crystallizes from hot glacial

acetic acid in aggregates of yellowish, monoclinic prisms melting at 256°, intumescing at higher temperatures, readily soluble in alkalis or glacial acetic acid, sparingly in alcohol or hot water and insoluble in ether, benzene or chloroform. It forms soluble alkali and alkali earth salts; the neutral barium salt crystallizes in yellowish scales; the silver derivative is a white precipitate, while the copper salt has the formula $(O_2N.C_6H_4)_2AsO.OCuOH$.

Di(4-nitrophenyl)arsinic acid is obtained by adding an alkaline solution of 4-nitrophenylarsenious acid to 4-nitrodiazonium chloride and acidifying with hydrochloric acid. The product separates as a yellowish precipitate difficultly soluble in water or alcohol but readily in alkalis.[86]

4-Aminophenylmethylarsinic acid, $\begin{matrix} CH_3 \diagdown \\ \quad AsO.OH \\ H_2N.C_6H_4 \diagup \end{matrix}$, results upon treating an alkaline solution of 4-aminophenylarsineoxide with methyl iodide, and isolating the free acid either through the silver salt, as in the case of phenylmethylarsinic acid, or by removing the iodine with freshly precipitated silver chloride and concentrating the acidified filtrate. It separates from alcohol-ether as a crystalline powder melting at 201°.[1268]

2-Aminodiphenylarsinic acid, $\begin{matrix} C_6H_5 \diagdown \\ \quad AsO.OH \\ H_2N.C_6H_4 \diagup \end{matrix}$, is obtained by reducing the corresponding nitro compound with ferrous sulfate and powdered iron in hot water. The free acid forms a snow-white, crystalline powder, m. p. 129-30°; easily soluble in alkalis, alcohol, glacial or hot dilute acetic acid, moderately so in hot benzene and difficultly in hot water.[1269]

2′-Aminodiphenylarsinic acid-2-arsonic acid, $\begin{matrix} H_2O_3AsC_6H_4 \diagdown \\ \quad AsO.OH. \\ H_2N.C_6H_4 \diagup \end{matrix}$ —The corresponding nitro compound is reduced with ferrous hydroxide, and the crude acid purified by dissolving in hydrochloric acid and neutralizing with sodium hydroxide and sodium acetate. It crystallizes in star-shaped aggregates of pale, rose-colored needles, and forms a soluble hydrochloride.[1270]

Di(3-aminophenyl)arsinic acid, $(H_2N.C_6H_4)_2AsO.OH$, is prepared from the corresponding dinitro compound like the preceding acid. It

crystallizes from dilute alcohol in faintly reddish leaflets easily soluble in dilute hydrochloric acid, from which the concentrated acid precipitates the crystalline hydrochloride.[1271]

Di(4-aminophenyl)arsinic acid results as a by-product in the preparation of p-arsanilic acid by Béchamp's reaction. Separation may be effected by dissolving the mixture of the two acids in hot caustic soda solution, decolorizing with animal charcoal, and precipitating the atoxyl with alcohol. After distilling off the alcohol from the filtrate, the secondary arsinic acid is obtained upon neutralizing with hydrochloric acid.[1272] Another method of separation consists in digesting the mixture with just sufficient aqueous caustic soda to give a faintly alkaline reaction with litmus, the p-arsanilic acid dissolving while the arsinic acid remains undissolved. The latter is converted into the corresponding barium salt, and the free acid obtained by neutralizing with hydrochloric acid.[1273] According to Kober[1274] the above arsinic acid may be obtained practically free of p-arsanilic acid by slowly heating a mixture of arsenic acid and an excess of aniline up to 230°, extracting with aqueous sodium hydroxide and precipitating with acetic acid. The crude product is then purified by dissolving in the least quantity of sodium hydroxide, removing the adhering aniline by steam distillation or aeration while boiling, slightly acidifying with acetic acid, adding a slight excess of acetic acid to the filtrate, and extracting the resulting precipitate with hot acetone, from which the arsinic acid separates on standing in a cold place. Upon recrystallization from 50 per cent acetic acid, it separates in felted needles, m. p. 232° (Benda), 248-9° (Pyman); soluble in excess of mineral acids, alkali hydroxides or carbonates, hot water, methyl or ethyl alcohol or glacial acetic acid, sparingly so in cold water and insoluble in ether, benzene or chloroform. With silver nitrate in neutral solution it forms a white precipitate soluble in ammonia or nitric acid. Upon boiling with sulfuric acid and potassium iodide it yields 4-iodoaniline, but no precipitate is obtained by boiling with magnesia mixture in ammoniacal solution (distinction from p-arsanilic acid). The sodium salt,

$$(H_2N.C_6H_4)_2AsO.ONa.5\text{-}6H_2O,$$

which is very soluble in alcohol or water, crystallizes from the latter in monoclinic plates melting at 83°, but on further heating it loses water, resolidifies and does not melt up to 250°. The barium salt,

$$[(H_2N.C_6H_4)_2AsO.O]_2Ba.7\tfrac{1}{2}H_2O,$$

crystallizes in prisms easily soluble in water but only sparingly in alcohol.

Di(4-amino-3-methylphenyl)arsinic acid,

$$[H_2N.C_6H_3(CH_3)]_2AsO.OH,$$

is obtained as a by-product in the arsenation of o-toluidine, and is separated from the primary arsonic acid in a manner similar to that described under the preceding compound.[944, 1275] The free acid crystallizes from hot water in highly refractive, microscopic needles melting at 247-9° with decomposition (Pyman), and from 35 per cent acetic acid in short prisms melting at 243° (Benda). It is readily soluble in excess of dilute alkalis or mineral acids, hot glacial acetic acid, methyl or ethyl alcohol, difficultly in hot water and practically insoluble in cold water, ether, acetone, benzene or chloroform. Upon boiling with dilute sulfuric acid and potassium iodide it yields 4-amino-3-methyliodobenzene; with both silver nitrate and magnesia mixture it reacts like di(4-aminophenyl)arsinic acid.

The sodium salt, $[H_2N.C_6H_3(CH_3)]_2AsO.ONa.7\frac{1}{2}H_2O$, forms prismatic needles melting at 74-5°; upon continued heating it loses water, resolidifies and does not remelt up to 250°. It is readily soluble in water or alcohol.[1276]

4-Acetylaminophenylmethylarsinic acid,

$$\left.\begin{array}{r} CH_3 \\ (CH_3CO.HN)C_6H_4 \end{array}\right\rangle AsO.OH,$$

results from the interaction of 4-acetylaminophenylarsineoxide and methyl iodide in alkaline solution. It crystallizes from hot water in prisms, m. p. 260° with decomposition; soluble in acetic acid, methyl or ethyl alcohol and insoluble in acetone or ethyl acetate.[1268]

Di(4-acetylaminophenyl)arsinic acid,

$$[(CH_3CO.HN)C_6H_4]_2AsO.OH.$$

Upon acetylating the corresponding diamino derivative, and recrystallizing from water, the product separates in rosets of needles containing $3H_2O$ and melting at 275° (Pyman). When recrystallized from 30 per cent acetic acid, however, it separates as a white, crystalline powder melting at 260-2° (Benda). It is readily soluble in mineral acids, dilute alkalis, sodium carbonate, ammonia, hot water, alcohol or glacial acetic acid, sparingly in cold water or the usual organic solvents, and yields no precipitate with magnesia mixture. Its sodium salt crystallizes from water in prismatic needles containing $9H_2O$ and melting at 50°, but the anhydrous salt does not melt up to 250°.[1277, 1278]

Di(4-acetylamino-3-methylphenyl)arsinic acid,

$$[(CH_3CO.HN)C_6H_3(CH_3)]_2AsO.OH,$$

crystallizes from hot water[1279] in highly refractive, microscopic prisms containing $\frac{2}{3}H_2O$ and melting at 242-4°, but separates from 25 per cent acetic acid in lustrous prisms which soften at 237° and decompose at 255° with frothing.[1280] It is insoluble in dilute mineral acids, cold water or the usual organic solvents, but dissolves readily in dilute alkalis or glacial acetic acid. Its sodium salt consists of silky needles containing $6H_2O$, melting at 106-7°, and soluble in water or alcohol. The anhydrous salt does not melt up to 250°.

Di(4-oxalylaminophenyl) arsinic acid,

$$[(HOOCCO.HN)C_6H_4]_2AsO.OH,$$

is prepared by heating sodium di(4-aminophenyl)arsinate with oxalic acid, first at 140°, until most of the water is driven off, and finally at 160°. The free acid, isolated through the barium salt, crystallizes in slender needles containing $4H_2O$, is sparingly soluble in boiling water, methyl or ethyl alcohol and practically insoluble in acetic acid.[1281]

Di(4-alkylaminophenyl) arsinic acids, $(RHN.C_6H_4)_2AsO.OH$, result upon warming monoalkylanilines with arsenic trichloride in pyridine for two hours at 115-20°, and oxidizing the resulting chloroarsines with hydrogen peroxide in acid or alkaline solution. The products thus obtained contain more or less of the corresponding arsonic acids, $RHN.C_6H_4AsO(OH)_2$, which may be removed by taking advantage of their insolubility in alcohol-ether mixture, in which the arsinic acids are soluble. In this way the methyl, ethyl and amyl derivatives have been prepared.[1282]

Bis(dibromo-3-aminophenyl) arsinic acid, $(H_2N.C_6H_2Br_2)_2AsO.OH$, melting at 187°. is derived from di(3-aminophenyl)arsinesulfide by warming with bromine water at boiling water-bath temperature.[1283]

Bis(tribromo-3-aminophenyl) arsinic acid, $(H_2N.C_6HBr_3)_2AsO.OH$, prepared like the preceding compound by warming over a free flame, separates as a brown mass, from which the pure product is obtained by dissolving in ammonia, clarifying with charcoal, and reprecipitating with hydrochloric acid. It forms a white powder more stable than the preceding compound, melts at 287°, is difficultly soluble in glacial acetic acid and insoluble in alcohol.[1283]

Di(3-nitro-4-aminophenyl) arsinic acid,

$$[(O_2N)(H_2N)C_6H_3]_2AsO.OH,$$

is a yellow crystalline powder very sparingly soluble in water or the usual organic solvents. It results upon nitrating di(4-oxalylaminophenyl)arsinic acid and hydrolyzing the resulting product. Upon warm-

ing with an excess of caustic potash the amino group is replaced by a hydroxyl.[1281]

Di(4-hydroxyphenyl)arsinic acid, $(HO.C_6H_4)_2AsO.OH$, is obtained from the corresponding diamino arsinic acid by diazotizing in mineral acid solution and warming until the evolution of nitrogen ceases.[1275, 1284] It also results as a by-product in the direct arsenation of phenol.[1285] It crystallizes from 50 per cent acetic acid in thin plates, m. p. 239° (Benda), 259° with decomposition (Fargher); readily soluble in alkali hydroxides or carbonates, hot water, methyl or ethyl alcohol, glacial acetic or normal hydrochloric acid, very sparingly in acetone or chloroform and insoluble in ether, benzene or ligroin. It yields no precipitate with magnesia mixture.

2,2′ or 2,4′-Di(hydroxyphenyl)arsinic acid, also obtained as a by-product in the arsenation of phenol, forms lustrous prisms, m. p. 215-6°; soluble in methyl alcohol, dilute hydrochloric acid, alkali hydroxides or carbonates, boiling water, ethyl alcohol or acetic acid, very sparingly so in acetone or ether and insoluble in benzene or chloroform. It couples with diazotized sulfanilic acid in alkaline solution, yielding an orange solution.[1286]

Di(4-hydroxy-3-methylphenyl)arsinic acid,

$$[HO.C_6H_3(CH_3)]_2AsO.OH,$$

prepared like the corresponding di(hydroxyphenyl) compound, separates from 75 per cent acetic acid as a colorless, crystalline powder, m. p. 247°; readily soluble in sodium hydroxide or carbonate, warm alcohol, glacial acetic or normal hydrochloric acid, sparingly in cold or warm water and insoluble in ether, benzene or ligroin. It is not precipitated by magnesia mixture.[1280]

3-Nitro-4-hydroxyphenylmethylarsinic acid,

$$\begin{array}{l} \quad CH_3 \\ \qquad\quad \diagdown \\ \qquad\qquad AsO.OH, \\ \qquad\quad \diagup \\ (O_2N)(HO)C_6H_3 \end{array}$$

obtained from 3-nitro-4-hydroxyphenylarsineoxide and methyl iodide in methyl alcoholic caustic soda, crystallizes from 50 per cent acetic acid in prisms, m. p. 232-3° with decomposition; easily soluble in glacial acetic acid or methyl alcoholic hydrochloric acid, difficultly in water or methyl alcohol and insoluble in ether, acetone, chloroform or benzene.[1260]

Di(3-nitro-4-hydroxyphenyl)arsinic acid,

$$[(O_2N)(HO)C_6H_3]_2AsO.OH,$$

may be produced either by nitrating di(4-hydroxyphenyl)arsinic acid at $-5°$ to $-3°$,[1284] or by warming di(3-nitro-4-aminophenyl)arsinic acid with an excess of caustic potash solution.[961] The product is almost insoluble in boiling water, fairly soluble in glacial acetic acid and sparingly so in 50 per cent acetic acid, from which it separates in rhomboidal prisms melting at 230° with decomposition.

3-Amino-4-hydroxyphenylmethylarsinic acid,

$$\begin{array}{l} \quad\quad\quad\quad\quad CH_3 \\ \quad\quad\quad\quad\quad\quad \diagdown \\ \quad\quad\quad\quad\quad\quad\quad AsO.OH. \\ \quad\quad\quad\quad\quad\quad \diagup \\ (H_2N)(HO)C_6H_3 \end{array}$$

Upon reducing the corresponding nitro compound with sodium hydrosulfite in alkaline solution up to 35°, then acidifying with hydrochloric acid, and recrystallizing from water, the amino compound is obtained in almost colorless needles melting at 206-7° with vigorous decomposition. It reduces Fehling's and Tollens' solutions, and with sodium nitrite yields a lemon-yellow, soluble diazo compound which couples with resorcin, producing a red coloration.[1287]

Di(3-amino-4-hydroxyphenyl)arsinic acid,

$$[(H_2N)(HO)C_6H_3]_2AsO.OH,$$

is a sandy, crystalline precipitate soluble in water or methyl alcohol but sparingly so in ethyl acetate. It is derived from the corresponding dinitro compound by reduction with sodium hydrosulfite in alkaline solution up to 30°.[758]

Di(3-methoxy-4-hydroxyphenyl)arsinic acid,

$$[(CH_3O)(HO)C_6H_3]_2AsO.OH,$$

obtained as a by-product in the preparation of 3-methoxy-4-hydroxyphenylarsonic acid, separates from water in radiating clusters of minute prisms containing $1\frac{1}{2}H_2O$, and melting at 234°. Its ammoniacal solution yields a precipitate on warming with barium chloride.[626]

Di(4-carboxyphenyl)arsinic acid (Di-p-benzarsinic acid),

$$(HOOC.C_6H_4)_2AsO.OH,$$

results upon oxidizing di(4-methylphenyl)arsinic acid with four molecular proportions of potassium permanganate in a moderately concentrated alkaline solution at 50-60°, and neutralizing the filtrate with hydrochloric acid. It crystallizes in lustrous leaflets decomposing at high temperatures without melting, is slightly soluble in hot concentrated hydrochloric acid or alcohol, practically insoluble in cold or hot water,

but dissolves readily in alkalis. Its salts crystallize poorly and consist of mixtures of neutral and acid salts. Upon heating the mixture of silver salts with methyl iodide in a sealed tube at 100°, and recrystallizing from alcohol, the methyl ester, $(CH_3OOC.C_6H_4)_2AsO.OH$, is obtained in pale yellow crusts, m. p. above 280°.[1288]

Phenylarsinoacetic acid,

$$\begin{array}{l} C_6H_5 \diagdown \\ \qquad AsO.OH, \\ HOOCCH_2 \diagup \end{array}$$

from phenyldichloroarsine and sodium chloroacetate in alkaline solution, melts at 141-2° with decomposition.[759]

Phenylarsinoacetanilide,

$$\begin{array}{l} C_6H_5 \diagdown \\ \qquad AsO.OH, \\ C_6H_5NHOCCH_2 \diagup \end{array}$$

from disodium phenylarsenite and chloroacetanilide, melts at 182-3° with gas evolution.[759]

Phenylarsinoacetphenetidine,

$$\begin{array}{l} C_6H_5 \diagdown \\ \qquad AsO.OH, \\ C_2H_5OC_6H_4NHOCCH_2 \diagup \end{array}$$

from disodium phenylarsenite and chloroacetphenetidine, crystallizes from alcohol in needles melting at 175° with decomposition.[760]

Phenylarsinoacetyl-p-arsanilic acid,

$$\begin{array}{l} C_6H_5 \diagdown \\ \qquad AsO.OH, \\ H_2O_3AsC_6H_4NHOCCH_2 \diagup \end{array}$$

from disodium phenylarsenite and chloroacetyl-p-arsanilate, is a white solid insoluble in water or the usual organic solvents, soluble in alkalis, and does not melt below 250°.[760]

Phenylarsino-2-acetylaminobenzoic acid,

$$\begin{array}{l} C_6H_5 \diagdown \\ \qquad AsO.OH, \\ HOOCC_6H_4NHOCCH_2 \diagup \end{array}$$

similarly prepared from o-chloroacetylaminobenzoate, is purified by boiling its alkaline solution with animal charcoal, filtering and reprecipi-

tating with hydrochloric acid. It melts at 198-200° with decomposition.[760]

β-Phenoxyethylphenylarsinic acid,

$$\begin{array}{l} C_6H_5 \diagdown \\ \qquad\qquad AsO.OH, \\ C_6H_5OCH_2CH_2 \diagup \end{array}$$

pre-pared by heating and stirring β-phenoxyethyl bromide with disodium phenylarsenite for four to six hours, melts at 122-3°.[760]

Ethylene diphenyldiarsinic acid,

$$\begin{array}{ccccc} & C_6H_5 & & C_6H_5 & \\ HO.OAs & & & & AsO.OH, \\ & CH_2 & - & CH_2 & \end{array}$$

separates as an oil on heating and stirring ethylene bromide with disodium phenylarsenite for four to eight hours. Upon dissolving in dilute ammonium hydroxide, filtering and reprecipitating by careful acidification with hydrochloric acid, an oil is obtained which gradually solidifies. It may be recrystallized from hot water or alcohol and melts at 209-11.[760]

4-Aminophenylarsinoacetic acid,

$$\begin{array}{l} H_2N.C_6H_4 \diagdown \\ \qquad\qquad AsO.OH. \\ HOOCCH_2 \diagup \end{array}$$

—An alkaline solution of 4-aminophenylarsineoxide is treated with chloroacetic acid and precipitated as the calcium salt, from which the free acid is isolated by boiling with dilute aqueous oxalic acid. The reaction proceeds according to the equation:

$$H_2N.C_6H_4AsO + CH_2ClCOONa + 2NaOH \longrightarrow$$

$$\begin{array}{l} H_2N.C_6H_4 \diagdown \\ \qquad\qquad AsO.OH + NaCl + H_2O. \\ NaOOCCH_2 \diagup \end{array}$$

The product crystallizes from dilute alcohol in platelets melting at 162° with gas evolution, readily soluble in water, alkalis, glacial acetic or mineral acids, methyl or ethyl alcohol and insoluble in acetone, ether or benzene. It exhibits all of the properties of a primary amine: it liberates iodine from hydriodic acid, and is decomposed by bromine water, yielding tribromoaniline and a primary arsonic acid.[1289]

4-Aminophenylarsinoacetanilide,

$$\begin{array}{l} H_2N.C_6H_4 \diagdown \\ \qquad\qquad AsO.OH, \\ C_6H_5NHOCCH_2 \diagup \end{array}$$

from

disodium-4-aminophenylarsenite and chloroacetanilide, melts at 181-2° with decomposition.[471]

4-Aminophenylarsinoacetphenetidine,

$$\begin{matrix} H_2N.C_6H_4 & & \\ & \searrow & \\ & & AsO.OH, \\ & \nearrow & \\ C_2H_5OC_6H_4NHOCCH_2 & & \end{matrix}$$

similarly prepared from chloroacetphenetidine, melts at 211.5-212.5°.[471]

4-Aminophenylarsinoacetyl-p-arsanilic acid,

$$\begin{matrix} H_2N.C_6H_4 & & \\ & \searrow & \\ & & AsO.OH, \\ & \nearrow & \\ H_2O_3AsC_6H_4NHOCCH_2 & & \end{matrix}$$

does not melt below 250°. It is made from sodium chloroacetyl-p-arsanilate and disodium 4-aminophenylarsenite.[1290]

4-Aminophenylarsino-4′-acetylaminobenzoic acid,

$$\begin{matrix} H_2N.C_6H_4 & & \\ & \searrow & \\ & & AsO.OH, \\ & \nearrow & \\ HOOCC_6H_4NHOCCH_2 & & \end{matrix}$$

is derived from sodium 4-chloroacetylaminobenzoate like the preceding compound. It crystallizes from hot water in needles, m. p. 217° with decomposition.[1290]

4-Acetylaminophenylarsinoacetanilide,

$$\begin{matrix} CH_3CONH.C_6H_4 & & \\ & \searrow & \\ & & AsO.OH, \\ & \nearrow & \\ C_6H_5NHOCCH_2 & & \end{matrix}$$

is obtained from the corresponding amino derivative by warming with a slight excess of acetic anhydride for 15 minutes after the initial reaction is over, and diluting with water. It crystallizes from hot water in plates, m. p. 205-6° with decomposition.[471]

4-Acetylaminophenylarsinoacetphenetidine,

$$\begin{matrix} CH_3CONH.C_6H_4 & & \\ & \searrow & \\ & & AsO.OH, \\ & \nearrow & \\ C_2H_5OC_6H_4NHOOCH_2 & & \end{matrix}$$

similarly prepared, melts at 214-5° with decomposition.[471]

4-Acetylaminophenylarsinoacetyl-p-arsanilic acid,

$$\begin{matrix} CH_3CONH.C_6H_4 \diagdown & \\ & AsO.OH, \\ H_2O_3AsC_6H_4NHOCCH_2 \diagup & \end{matrix}$$

does not melt below 250°.[1290]

4-Glycylaminophenylarsinoacetanilide,

$$\begin{matrix} HOOCCH_2NH.C_6H_4 \diagdown & \\ & AsO.OH, \\ C_6H_5NHOCCH_2 \diagup & \end{matrix}$$

from 4-aminophenylarsinoacetanilide and chloroacetic acid in alkaline solution by refluxing for three-four hours, melts at 199° with decomposition.[471]

C. Tertiary Derivatives.

1. *Tertiary Arsine Dihalides, Oxyhalides and Cyanohalides.*—Tertiary arsines readily combine additively with halogens either directly or in the presence of anhydrous solvents, forming the corresponding dihalides:

$$R_3As + X_2 \longrightarrow R_3AsX_2.$$

The tribenzylarsine diiodide, however, has been prepared by the action of hydriodic acid upon an alcoholic solution of tribenzylarsine oxide.

The dihalides consist of crystalline solids which are very sensitive to the action of moisture, yielding the corresponding hydroxyhalides:

$$R_3AsX_2 + H_2O \longrightarrow R_3As(OH)X + HX.$$

With alkalis, however, they form either the corresponding arsine oxides or dihydroxides:

$$R_3AsX_2 + 2NaOH \begin{cases} \nearrow R_3As(OH)_2 + 2NaX \\ \searrow R_3AsO + 2NaX + H_2O \end{cases}$$

In many cases they combine with an excess of halogen, yielding the corresponding tetrahalides, while with alkyl iodides in a sealed tube at 100°, they often form arsonium compounds. Dihalides containing one or two aliphatic and two or one aromatic radicals respectively

attached to the arsenic, decompose upon heating into an alkylhalide and a secondary halogenated arsine:

$$RR'_2AsX_2 \longrightarrow R'_2AsX + RX$$
$$R_2R'AsX_2 \longrightarrow RR'AsX + RX$$

(where R = an alkyl and R′ an aryl group).

The hydroxyhalides are formed:

1. Upon treating tertiary arsineoxides or dihydroxides with haloid acids:

$$R_3AsO + HX \longrightarrow R_3As.OH.X$$
$$R_3As(OH)_2 + HX \longrightarrow R_3As.OH.X + H_2O.$$

2. From the corresponding dihalides when treated with water:

$$R_3AsX_2 + H_2O \longrightarrow R_3As.OH.X + HX.$$

The isolation of the dihalide is not essential, as the hydroxyhalides are formed directly upon adding halogen to a tertiary arsine in a moist solvent.

3. By the action of moisture upon triaryl cyanohalides:

$$R_3As\begin{matrix}\diagup CN\\ \diagdown X\end{matrix} + H_2O \longrightarrow R_3As.OH.X + HCN.$$

The compounds are crystalline solids generally soluble in water or alcohol. They react with silver nitrate to form silver halides and the corresponding triarylarsine hydroxynitrates:

$$R_3As.OH.X + AgNO_3 \longrightarrow R_3As.OH.NO_3 + AgX;$$

while with picric acid they yield the corresponding hydroxy picrates:

$$R_3As.OH.X + HO.C_6H_2(NO_2)_3 \longrightarrow R_3As.OH.OC_6H_2(NO_2)_3 + HX.$$

A hydroxychromate has been obtained by treating triphenylarsine hydroxychloride with potassium chromate. When heated at high temperatures either under reduced or atmospheric pressure, the hydroxybromides are decomposed into various arsenical and non-arsenical compounds, the decomposition being analogous to that occurring when trialkylammonium hydroxyhalides are heated either alone or with alcoholic potash.

Tertiary arsines, unlike the analogous amines, combine additively with cyanogen halides in the complete absence of moisture to form the corresponding arsine cyanohalides:

$$R_3As + CNX \longrightarrow R_3As\begin{matrix}\diagup CN\\ \diagdown X\end{matrix}.$$

This property, however, may be completely destroyed by introducing strongly negative radicals into the nucleus.

The resulting crystalline products are extremely sensitive to moisture, which transforms them into hydroxyhalides, but are decomposed by heat only at elevated temperatures. Thus triphenylarsine cyanobromide decomposes upon heating into its components together with small amounts of cyanogen bromide, triphenylarsine hydroxybromide and an unidentified brown powder containing nitrogen. This decomposition is similar to that of the corresponding phosphorus derivative, which proceeds according to the equation:

$$2(C_6H_5)_3P\begin{matrix}\diagup Br\\ \diagdown CN\end{matrix} \longrightarrow (CN)_2 + (C_6H_5)_3P + (C_6H_5)_3PBr_2.$$

The mixed aliphatic-aromatic arsine cyanobromides, however, yield an alkyl bromide and a secondary cyanoarsine:

$$RR'R''As\begin{matrix}\diagup CN\\ \diagdown X\end{matrix} \longrightarrow R''X + RR'AsCN$$

(where R'' = an alkyl radical). If more than one alkyl group is present, the smallest radical is invariably split off in the above reaction.

The greater stability of the arsine cyanobromides towards heat as compared with the corresponding amines is due to the more metallic, and therefore more positive, character of the arsenic.

Phenyldimethylarsine dichloride, $C_6H_5(CH_3)_2AsCl_2$, separates upon passing chlorine into a cold petroleum ether solution of the corresponding arsine. It melts at 134° with decomposition.[227]

The corresponding *dibromide,* prepared by adding bromine to an excess of phenyldimethylarsine in petroleum ether, is a white, crystalline, slightly hygroscopic compound melting at 128° with violent decomposition. With more bromine the above arsine yields the *tetrabromide,* $C_6H_5(CH_3)_2AsBr_4$, dark red crystals melting at 61° and decomposing at 160° into phenyldibromoarsine and methyl bromide.[734]

The *hydroxychloride,* $C_6H_5(CH_3)_2.AsOH.Cl$, is obtained as white needles, m. p. 163°, upon treating an alcoholic solution of the corresponding arsine dihydroxide with concentrated hydrochloric acid.[1291] The *hydroxybromide* results upon exposing the corresponding cyanobromide to the air, or upon mixing ethereal solutions of phenyldimethylarsine and cyanogen bromide in the presence of air. It crystallizes from

acetone in lustrous needles, m. p. 162°; soluble in water, pyridine, nitrobenzene, phenol, methyl or ethyl alcohol, slightly so in benzene, toluene or cold acetone and insoluble in ether, ligroin or carbon bisulfide. It reacts quantitatively with aqueous silver nitrate, yielding silver bromide, and with picric acid it forms a hydroxypicrate,

$$C_6H_5(CH_3)_2As(OH)[O.C_6H_2(NO_2)_3],$$

which crystallizes from alcohol in needles melting at 132°.[1292] When gradually heated up to 178° in an atmosphere of nitrogen at 13-15 mm. pressure, the hydroxybromide decomposes into phenyltrimethylarsonium bromide, phenylmethylarsinic acid, phenylmethylbromoarsine, and small quantities of phenyldimethylarsine, phenyldibromoarsine, methylbromide, methyl alcohol and water. When heated up to 195° in a nitrogen atmosphere at ordinary pressure, the products obtained are phenyltrimethylarsonium bromide, phenylmethylbromoarsine, phenyldimethylarsine, methyl bromide, methyl alcohol, hydrobromic acid, diphenylbromoarsine and arsenic trioxide.[1293] The *hydroxyiodide* is prepared like the corresponding bromine compound, employing cyanogen iodide. It crystallizes in yellow needles, m. p. 117°; easily soluble in water, alcohol or acetone, sparingly in hot benzene or carbon tetrachloride and insoluble in ether or ligroin.[1294]

Phenyldiethylarsine dichloride, $C_6H_5(C_2H_5)_2AsCl_2$, is obtained like the corresponding dimethyl compound.[1295] The *dibromide* is a white, crystalline mass melting at 85° with decomposition, and rapidly decomposing at 120° into phenylethylbromoarsine and ethyl bromide,[735] while the *diiodide* is a yellow, microcrystalline substance melting at 95° and decomposing at 105°. It results upon treating phenyldiethylarsine with iodine in petroleum ether solution.[803]

Phenylmethylethylarsine hydroxybromide,

$$(C_6H_5)(CH_3)(C_2H_5)As.OH.Br,$$

is a white, crystalline mass, m. p. 83°, prepared from the corresponding arsine and cyanogen bromide without the exclusion of atmospheric moisture. When treated with picric acid it forms the corresponding hydroxypicrate, a light yellow crystalline powder, m. p. 113.5°.[800]

Phenylmethyl-n-propylarsine hydroxybromide,

$$(C_6H_5)(CH_3)(C_3H_7)As.OH.Br,$$

m. p. 146°, is obtained like the preceding compound. Its hydroxypicrate consists of needles, m. p. 84°.[762]

Diphenylmethylarsine hydroxybromide, $(C_6H_5)_2(CH_3)As.OH.Br$, crystallizes from acetone in lustrous, refractive crystals, m. p. 118°;

readily soluble in water, alcohol or hot acetone, difficultly in carbon bisulfide and insoluble in ether or ligroin. The corresponding hydroxypicrate melts at 137°.[1296]

Phenylbenzylmethylarsine hydroxybromide,

$$(C_6H_5)(C_6H_5.CH_2)(CH_3)As.OH.Br,$$

is a microcrystalline powder melting at 147°. The hydroxypicrate consists of yellow needles, m. p. 119°.[1297]

Diphenylethylarsine dichloride, $(C_6H_5)_2(C_2H_5)AsCl_2$, results upon passing chlorine into diphenylethylarsine. It consists of colorless needles, m. p. 137°; fumes slightly in air, is easily decomposed by water, yielding hydrochloric acid, and when heated with ethyl iodide in a sealed tube at 100°, forms diphenyldiethylarsonium iodide.[1298]

The *hydroxybromide,* $(C_6H_5)_2(C_2H_5)As.OH.Br$, exists as white crystals melting at 97.5°. With picric acid it forms a hydroxypicrate, lustrous lemon-yellow leaflets, m. p. 116°.[268]

Phenyl-p-tolylethylarsine dichloride,

$$(C_6H_5)(C_6H_4.CH_3)(C_2H_5)AsCl_2,$$

crystallizes from benzene in white needles, m. p. 148°.[809]

Triphenylarsine dichloride, $(C_6H_5)_3AsCl_2$, results from the interaction of triphenylarsine and chlorine. When recrystallized from hot benzene it separates in colorless plates sintering at 158°, melting at 204-5°, and readily soluble in water or alcohol. It is very unstable in moist air, forming the hydroxychloride. At 280° it decomposes into diphenylchloroarsine and chlorobenzene: [1299]

$$(C_6H_5)_3AsCl_2 \longrightarrow (C_6H_5)_2AsCl + C_6H_5Cl.$$

The *dibromide,* similarly prepared, forms white crystals sintering at 165°, melting at 215°, and is as unstable as the dichloride.[1300] The *diiodide,* obtained from triphenylarsine and iodine in petroleum ether with the exclusion of atmospheric moisture, is an unstable yellow to orange-yellow powder melting at 130-40°. When heated with methyl iodide in a sealed tube at 100° for three hours, it forms triphenylmethylarsonium iodide.[767] The *tetraiodide,* $(C_6H_5)_3AsI_4$, is obtained in steel-blue needles, m. p. 142-4°, by the interaction of iodine and triphenylarsine in carbon tetrachloride solution.[1301] The *dibromodiiodide,* $(C_6H_5)_3AsBr_2.I_2$, forms yellowish-red needles, m. p. 120-1°, upon adding the corresponding amounts of bromine and iodine to a chloroform solution of triphenylarsine.[1301]

The *hydroxychloride*, $(C_6H_5)_3As.OH.Cl$, may be obtained either by treating the dichloride with water, or by passing chlorine into a solution of triphenylarsine in commercial chloroform.[1302] It exists as vitreous crystals, m. p. 171°, easily soluble in water or alcohol. Its platinichloride, $[(C_6H_5)_3As.OH.Cl]_2PtCl_4$, consists of yellow needles melting at 180-2°. With potassium chromate, it forms a yellowish-red precipitate of the hydroxychromate, $(C_6H_5)_3As.OH(O.CrO_3H)$. The *hydroxybromide* results from the interaction of cyanogen bromide and triphenylarsine in commercial ether. It forms lustrous crystals, m. p. 168°; easily soluble in alcohol, chloroform or hot acetone, difficultly in water, or carbon bisulfide, insoluble in ether or ligroin,[1303] and decomposes upon heating up to 240-50° under diminished pressure,[1304] yielding bromobenzene, triphenylarsine, diphenylbromoarsine, hydrobromic acid and water. The hydroxypicrate crystallizes in yellow needles melting at 162-3°.[1305]

Tri(3-methylphenyl)arsine hydroxychloride, $(CH_3.C_6H_4)_3As\begin{matrix}\diagup OH\\ \diagdown Cl\end{matrix}$, is prepared by treating the tertiary arsine with chlorine in the presence of hot water, forming beautiful crystals, m. p. 205°; easily soluble in alcohol but insoluble in ether or ligroin.[1306] The *hydroxybromide*, resulting from the action of bromine upon a chloroform solution of the arsine, separates as rhombic crystals, m. p. 190°, soluble in alcohol.[1307]

Diphenyl-4-methylphenylarsine dibromide, $\begin{matrix}(C_6H_5)_2\diagdown\\ (CH_3.C_6H_4)\diagup\end{matrix}AsBr_2$, is derived from the tertiary arsine and bromine in hot glacial acetic acid medium.[1308]

Phenyldi(4-methylphenyl)arsine dichloride, $\begin{matrix}(CH_3.C_6H_4)_2\diagdown\\ (C_6H_5)\diagup\end{matrix}AsCl_2$, forms a hard, transparent mass sintering at 186° and melting at 194°, when a chloroform solution of the arsine is saturated with chlorine, the excess of the latter removed by a current of carbon dioxide, and the solution evaporated in vacuo. Its platinichloride consists of crystals, m. p. 201°.[1309]

The *hydroxychloride*, $\begin{array}{ccc} (CH_3.C_6H_4)_2 & & OH \\ & \diagdown\!\!\diagdown \ \diagup & \\ & As & \\ & \diagup \ \diagdown & \\ C_6H_5 & & Cl \end{array}$, is obtained from the dichloride by the action of atmospheric moisture as a white powder soluble in alcohol or hot water, insoluble in ether, and melting at 142-3°. The *hydroxybromide* is similarly prepared.[1310]

Tri(4-methylphenyl)arsine dichloride, $(CH_3.C_6H_4)_3AsCl_2$, is a white, crystalline substance, m. p. 228-230°, derived from the tertiary arsine and chlorine in chloroform medium.[1311] The *dibromide*, consisting of white crystals, m. p. 245°, is formed from its components in carbon tetrachloride containing a little absolute ether.[1312] The *diiodide*, reddish needles, m. p. 172°, is similarly obtained by employing a dilute iodine solution. With an excess of iodine, however, the *tetraiodide* is formed as steel gray needles, m. p. 153°.[1312]

The *hydroxychloride* consists of white, feathery crystals, m. p. 185°. It results on hydrolyzing the dichloride with hot water, and may be recrystallized from chloroform or ether.[1313]

Tribenzylarsine dichloride, $(C_6H_5.CH_2)_3AsCl_2$, is formed along with tribenzylarsine and dibenzylarsinetrichloride by the interaction of benzyl chloride, arsenic trichloride and sodium in dry ether containing a little ethyl acetate. It has not been isolated.[826] The *diiodide*, prepared by the action of hydriodic acid upon the arsine oxide in alcoholic solution, separates as a pale yellow precipitate, m. p. 95°.[1314]

The *hydroxychloride*, $(C_6H_5.CH_2)_3As\begin{array}{l} \diagup OH \\ \diagdown Cl \end{array}$, consists of colorless crystals, m. p. 162-3°, derived from the arsine oxide by the action of dilute hydrochloric acid.[1315] The *hydroxybromide* is similarly obtained as colorless, tabular crystals, melting at 128-9°,[1314] while the *hydroxy-iodide*, prepared either by recrystallizing the diiodide from alcohol, or by the interaction of tertiary arsine and iodine in commercial ether, consists of colorless, tetragonal plates melting at 78°, and decomposing very readily with the liberation of hydriodic acid. The *hydroxynitrate* crystallizes in white needles, m. p. 170° with decomposition.[1314]

Tri(4-ethylphenyl)arsine dichloride, $(C_2H_5.C_6H_4)_3AsCl_2$, melts at 246°, and the *dibromide* at 212°.[833]

Phenyldi(2,4-dimethylphenyl)arsine dichloride,

$$(C_6H_5)[(CH_3)_2C_6H_3]_2AsCl_2,$$

is a very deliquescent substance, m. p. 176°; the *tetraiodide* consists of red-violet crystals, m. p. 127°, while the *hydroxychloride* melts at 186°.[1316]

Tri(2,5-dimethylphenyl)arsine dichloride, $[(CH_3)_2C_6H_3]_3AsCl_2$, has been prepared.[831]

Phenyldi(2,4,5-trimethylphenyl)arsine dichloride,

$$\begin{array}{l} C_6H_5 \\ \quad\quad \diagdown \\ \quad\quad\quad AsCl_2, \\ \quad\quad /\!\!/ \\ [C_6H_2(CH_3)_3]_2 \end{array}$$

is a crystalline powder, m. p. 217°, precipitated by adding ether to a carbon tetrachloride solution of the arsine saturated with chlorine. The *dibromide* is a deliquescent, crystalline solid, while the *diiodide* consists of yellowish-red crystals, m. p. 163.5°.

The *hydroxychloride,* obtained from the arsine and chlorine in commercial chloroform, forms transparent crystals, m. p. 173-5°. The *hydroxybromide,* m. p. 177°, and the *hydroxyiodide,* a pale yellow precipitate melting at 153°, have also been prepared.[1317]

Tri(2,4,5-trimethylphenyl)arsine dibromide, $[(CH_3)_3C_6H_2]_3AsBr_2$.—A yellow powder, m. p. 224-5°, derived from the tertiary arsine and bromine in ligroin. It is insoluble in organic solvents, and may be hydrolyzed by water to the *hydroxybromide,* m. p. 108°.[1318]

Tri(2,4,6-trimethylphenyl)arsine dibromide is prepared like the preceding isomer, and crystallizes from alcohol as well-defined rhombic crystals, m. p. 237°; readily soluble in chloroform or alcohol, and insoluble in ether.[1319] The *hydroxychloride* consists of white prisms, m. p. 100°, obtained on evaporating a solution of the arsine saturated with chlorine.[834]

Tri(4-isopropylphenyl)arsine dichloride, $[(CH_3)_2CH.C_6H_4]_3AsCl_2$.—White needles, m. p. 276°, made by passing chlorine into a chloroform solution of the arsine. Its platinichloride $[(C_9H_{11})_3AsCl_2]_2PtCl_6$, crystallizes from hot alcoholic hydrochloric acid in golden-yellow needles. The *dibromide,* needles melting at 142°, is prepared like the dichloride.[1320]

Tri(tertiary-butylphenyl)arsine dichloride, $[(CH_3)_3C.C_6H_4]_3AsCl_2$, is similarly obtained. If, however, alcohol is added to the chloroform solution of the arsine, the *hydroxychloride* results.[837]

Tri(4-phenylphenyl)arsine dichloride, $(C_6H_5.C_6H_4)_3AsCl_2$, m. p. 262°, is produced by the interaction of the arsine and chlorine in carbon tetrachloride solution. The *dibromide* is obtained in the same way, and melts at 168°. The *hydroxychloride,* m. p. 96°, and the *hydroxybromide,* sintering at 90° and melting at 145°, are similarly prepared, employing commercial chloroform as the solvent.[1321]

Tri-α-naphthylarsine dibromide, $(C_{10}H_7)_3AsBr_2$, separates as a dark brown resinous mass, which cannot be purified, upon adding bromine to a benzene solution of the arsine. When an excess of bromine is added to a chloroform solution of the arsine, the *tetrabromide* is obtained as a powder, m. p. 180°, which apparently contains two bromine atoms attached to the arsenic and the other two to the naphthalene nucleus. The corresponding *tetrachloride* is a white powder, m. p. 144°.[1322]

The *hydroxybromide,* pale brown crystals melting at 155°, is formed either on adding alcohol to the above impure dibromide or on rendering a benzene solution of the arsine turbid with alcohol, clarifying by means of a calculated quantity of bromine, concentrating to one-half of the volume and allowing to cool.[1322]

Tri-β-naphthylarsine dibromide is tarry, and cannot be obtained pure.[839]

Tri(3-nitrophenyl)arsine dibromide, $(O_2N.C_6H_4)_3AsBr_2$, results on treating a chloroform solution of the arsine with bromine. It is a reddish-yellow precipitate, m. p. 204°; easily soluble in glacial acetic acid.[1323]

Tri(?-chloro-3-nitrophenyl)arsine dichloride, $(O_2N.Cl.C_6H_3)_3AsCl_2$, is deposited as colorless crystals, m. p. 228°, when a chloroform solution of tri-(3-nitrophenyl)arsine is allowed to stand in a closed vessel in contact with chlorine. It is readily soluble in glacial acetic acid and sparingly in chloroform. The chlorine attached to the arsenic may be removed by treatment with silver nitrate in glacial acetic acid solution. The *dibromide* is a yellow substance melting at 209° and soluble in glacial acetic acid. It is formed from tri(chloro-3-nitrophenyl) arsine and bromine in chloroform solution.[1324]

Tri(?-chloro-3-nitro-4-methylphenyl)arsine dichloride,

$$(O_2N.Cl.CH_3.C_6H_2)_3AsCl_2,$$

precipitates on passing chlorine into a chloroform solution of tri(3-nitro-4-methylphenyl)arsine, and may be recrystallized from alcohol-chloroform. It melts at 170°, is easily soluble in alcohol but sparingly in chloroform.[847]

4-Carboxyphenyldiethylarsine dichloride, $\begin{matrix}(HOOC.C_6H_4) & \\ & \diagdown \\ & AsCl_2 \\ & /\!/ \\ (C_2H_5)_2 & \end{matrix}$, as well as the *dibromide* and *diiodide* are prepared from the corresponding arsine and the respective halogen in chloroform medium. By evaporating off the solvent they may be obtained in the form of crystals which are readily converted by moisture into the corresponding hydroxyhalides. The latter may be obtained pure by recrystallizing from alcohol.[1325]

4-Carboxyphenyldiethylarsine hydroxychloride,

$$\begin{matrix}(HOOC.C_6H_4) & & OH \\ & \diagdown \quad / & \\ & As & \\ & /\!/ \quad \diagdown & \\ (C_2H_5)_2 & & Cl\end{matrix},$$

may also be produced by shaking 4-methylphenyldiethylarsine with aqueous potassium permanganate, at first in the cold and finally at 30-40°. The arsine is first oxidized to the oxide, and the methyl group then converted into a carboxyl. After completely decolorizing the liquid with a few drops of alcohol and filtering off the manganese dioxide, the filtrate is acidified with hydrochloric acid and the solution evaporated to dryness. Upon extracting the residue with alcohol and evaporating the extract, a thick syrup remains which upon cooling solidifies to a crystalline mass. This may be purified by dissolving in absolute alcohol and reprecipitating with anhydrous ether, forming small, white crystals, m. p. 162°, soluble in water or alcohol and insoluble in ether. With mercuric chloride in concentrated aqueous solution it forms a crystalline double salt, $[(HOOC.C_6H_4)(C_2H_5)_2As.OH.Cl]HgCl_2$, which is readily soluble in hot alcohol, difficultly so in water, and melts at 182°. On passing hydrogen sulfide into an aqueous solution of the hydroxychloride, the corresponding arsinesulfide, $\begin{matrix}(C_2H_5)_2 & \\ & \diagdown\!\!\diagdown \\ & AsS \\ & / \\ HOOC.C_6H_4 & \end{matrix}$, m. p. 184°, precipitates.[1325] The *hydroxybromide* crystallizes in white needles, m. p. 144-5°, and the *hydroxyiodide* as brown leaflets, m. p. 84°.[1326]

Ethyl ester of 4-carboxytriphenylarsine dichloride,

$$\begin{matrix}(C_6H_5)_2 & \\ & \diagdown\!\!\diagdown \\ & AsCl_2, \\ & / \\ C_2H_5OOC.C_6H_4 & \end{matrix}$$

results on saturating an alcoholic solution of the corresponding arsine oxide with hydrogen chloride and evaporating. Beautiful, white crystals, m. p. 133°.[1327]

Diethyl ester of 4,4′-dicarboxytriphenylarsinedichloride,

$$\begin{array}{l} (C_6H_5)\diagdown \\ \qquad\qquad AsCl_2, \\ (C_2H_5OOC.C_6H_4)_2 /\!\!/ \end{array}$$

is similarly prepared from the arsine oxide and hydrogen chloride. The greater portion of the alcohol is distilled off, and the residue allowed to evaporate in a desiccator. It crystallizes from alcohol as warty aggregates of needles, m. p. 176°, having a pungent, but not a disagreeable odor.[1328]

Ethyl ester of 4-carboxy-4′-methyltriphenylarsine dichloride,

$$\begin{array}{r} C_6H_5 \diagdown \\ CH_3.C_6H_4 - AsCl_2, \\ C_2H_5OOC.C_6H_4 \diagup \end{array}$$

which is made like the preceding esters, melts at 94°, is soluble in alcohol and very hygroscopic.[824]

Phenyldimethylarsine cyanobromide, $\begin{array}{l} (CH_3)_2 \diagdown\!\!\diagdown \\ \qquad As.Br.CN, \\ (C_6H_5) \diagup \end{array}$ is produced by the interaction of the tertiary arsine and cyanogen bromide in ligroin solution in the complete absence of moisture. It is a white, microcrystalline powder melting at 94-6° with decomposition, and decomposing very quickly in the air with the formation of the corresponding hydroxybromide. On heating to 140° the compound breaks up into methyl bromide, phenyltrimethylarsonium bromide and phenylmethylcyanoarsine.[1292, 1294] The *cyanoiodide* is similarly obtained from cyanogen iodide, employing ether as a solvent. It exists as a yellow, finely crystalline powder, m. p. 93°, which is converted into the hydroxyiodide, m. p. 117°, on exposure to air.[1294]

Upon attempting to isolate phenylmethylethylarsine cyanobromide and phenylmethyl-n-propylarsine cyanobromide, immediate decomposition occurs, yielding methyl bromide and the respective cyanoarsines.[1329]

Diphenylmethylarsine cyanobromide, $(CH_3)(C_6H_5)_2As(CN)Br$.—From diphenylmethylarsine and cyanogen bromide in the usual manner. The product is a white, extremely light crystalline powder, m. p. 61-2°, which on exposure to air melts and then resolidifies to form the hydroxybromide. On heating the cyanobromide up to 100° it splits into methyl bromide and diphenylcyanoarsine.[1296, 1303]

Diphenylethylarsine cyanobromide, $(C_6H_5)_2(C_2H_5)As.CN.Br$, is made in the same general way, and exists as a white solid melting at 75° and unstable toward moisture. On gradually heating to about 140°, it splits into ethylbromide and diphenylcyanoarsine.[1330]

Triphenylarsine cyanobromide, $(C_6H_5)_3As(CN)Br$, prepared as above, is a white crystalline substance which begins to sinter at 120° and melts indefinitely at 130-40°. Moisture converts it into the corresponding *hydroxybromide,* while heating gradually to 175° breaks it up into a small quantity of cyanogen bromide, cyanogen, triphenylarsine, triphenylarsine hydroxybromide and an insoluble brown unidentified powder.[1331]

2. *Triarylarsine Dihydroxides and Oxides,* $R_3As(OH)_2$ and R_3AsO.—The corresponding arsine dihalides or hydroxyhalides readily exchange their halogens for hydroxyls when treated with water, caustic alkalis or ammonia:

$$R_3AsX_2 + 2NaOH \longrightarrow R_3As(OH)_2 + 2NaX$$
$$R_3As.OH.X + NaOH \longrightarrow R_3As(OH)_2 + NaX.$$

It is, however, unnecessary to isolate the above halogenated compounds, as treating a tertiary arsine successively with halogens and alkali gives the same results. The hydroxyhalides yield the same products on treatment with moist silver oxide:

$$R_3As.OH.X + AgOH \longrightarrow R_3As(OH)_2 + AgX.$$

The arsineoxides may be obtained in many cases from arsine dihalides or hydroxyhalides and alkalis; by dehydrating dihydroxides:

$$R_3As(OH)_2 \longrightarrow R_3AsO + H_2O;$$

or by combining tertiary arsines with sulfur monochloride, and decomposing the resulting addition products with water:

$$R_3As \xrightarrow{S_2Cl_2} R_3As\begin{matrix} \diagup Cl \\ \diagdown S.S.Cl \end{matrix} \xrightarrow{H_2O} R_3AsO + 2HCl + S_2.$$

The unsubstituted dihydroxides and arsineoxides are, as a rule, white or colorless crystalline solids soluble in alcohol and either sparingly so or entirely insoluble in water. They possess basic properties, forming hydroxy salts with acids such as nitric or picric. In many cases the oxides yield the corresponding sulfides with hydrogen sulfide, while with nascent hydrogen tertiary arsines result.

Tri(nitroaryl)arsine oxides are obtained from tertiary arsines by the action of a nitric-sulfuric acid mixture, nitration and oxidation occurring at the same time. A tri(aminophenyl)arsine oxide has been obtained directly from aniline and arsenic trichloride, and a tri(sulfophenyl)arsine oxide from triphenylarsine and concentrated sulfuric acid, the latter acting both as a sulfonating and oxidizing agent. Carboxylated triarylarsine oxides or dihydroxides result upon oxidizing tertiary arsines containing nuclear alkyl groups with either potassium permanganate at 50-60° for several weeks or, more rapidly, with nitric acid in a sealed tube. The latter compounds, generally crystalline, are sparingly soluble in water, more readily soluble in alcohol, and form water-soluble salts with alkalis.

Phenyldimethylarsine dihydroxide, $\begin{matrix} C_6H_5 \diagdown \\ (CH_3)_2 \diagup\!\!\diagup \end{matrix} As(OH)_2$, is a very hygroscopic substance resulting on treating an aqueous solution of the hydroxybromide with freshly precipitated silver oxide. With alcoholic picric acid it yields the corresponding hydroxypicrate.[1291]

Phenyl-α-naphthylmethylarsine oxide, $\begin{matrix} C_6H_5 \diagdown \\ C_{10}H_7 - \\ CH_3 \diagup \end{matrix} AsO$.—The corresponding tertiary arsine and bromine are allowed to react in chloroform at low temperature, the resulting solution shaken with a slight excess of aqueous caustic soda, and the chloroform layer removed and evaporated to dryness. The product crystallizes from toluene as colorless, well-defined prisms, m. p. 175°.[806]

Triphenylarsine dihydroxide, $(C_6H_5)_3As(OH)_2$, is derived from its dichloride by boiling with water or dilute ammonia;[1332] from the hydroxychloride by treatment with ammonia;[1301] or from the dibromide by boiling with concentrated aqueous caustic soda.[1333] Another method consists in refluxing a carbon bisulfide solution of the arsine with sulfur monochloride on a water-bath for one hour, evaporating off the solvent, boiling the residue with water, concentrating the turbid filtrate, and precipitating with ammonia.[820] The compound forms colorless plates, white needles or hexagonal prisms, m. p. 115-6°; soluble in water or alcohol, difficultly in ether. Nascent hydrogen reduces it to the arsine. On treating its dilute aqueous solution with nitric acid, the hydroxy nitrate, $(C_6H_5)_3As(OH)NO_3$, is obtained as long, lustrous needles, m. p. 160-1° (M.), while on dissolving the dihydroxide or oxide in concentrated nitric acid and evaporating to dryness on a water-bath, the nitrate, $(C_6H_5)_3As(NO_3)_2$, is obtained in the form of radiating aggregates readily affected by atmospheric moisture, and melting at 99-100°.

The corresponding *oxide,* $(C_6H_5)_3AsO$, is formed from the dihydroxide either by allowing it to stand over sulfuric acid; by heating at 105-10°;[1334] or by keeping it in vacuo for two hours.[766] It melts at 189°, and forms a yellow amorphous molybdate upon dissolving in boiling dilute aqueous sodium molybdate and acidifying with hydrochloric acid.[1335]

Tri(3-methylphenyl)arsine oxide, $(CH_3.C_6H_4)_3AsO$, is a white, crystalline mass, m. p. 170°; easily soluble in alcohol, though sparingly so in ether. It is produced by warming the arsine with an excess of bromine under water, and subsequently boiling with sodium hydroxide solution until decolorization occurs.[1307]

Diphenyl-4-methylphenylarsine dihydroxide, $\begin{matrix}(C_6H_5)_2 \diagdown \\ As(OH)_2 \\ (C_7H_7) \diagup\end{matrix}$, is derived from the dibromide by boiling with an excess of aqueous caustic potash. When crystallized from a benzene-ether solution, it melts at 68°, and is easily soluble in alcohol. Warming with dilute nitric acid produces the hydroxynitrate, white needles from alcohol-ether, m. p. 125°.[1308]

Phenyldi(4-methylphenyl)arsine oxide, $\begin{matrix}(C_6H_5) \diagdown \\ AsO \\ (C_7H_7)_2 \diagup\end{matrix}$.—From the corresponding halides by means of alkali. It is a white powder, m. p. 81°, which on warming with dilute nitric acid yields the hydroxynitrate, rosets of intertwined needles, m. p. 94°.[1310]

Tribenzylarsine oxide, $(C_6H_5.CH_2)_3AsO$, is obtained by the action of caustic soda upon the hydroxychloride.[1336] Recrystallized from dilute alcohol, it forms colorless, highly refractive prisms, m. p. 219-20°; readily soluble in alcohol or glacial acetic acid, less so in hot water and sparingly in cold water, ether or benzene. With the haloid acids, as well as with nitric acid, it forms hydroxy salts readily soluble in alcohol but practically insoluble in water or ether. The oxide is reduced to the arsine by means of zinc and glacial acetic acid containing concentrated hydrochloric acid, the reduction being best carried out at 50-60°. Boiling with red phosphorus and hydriodic acid converts it into tetrabenzylarsonium iodide.

Tri(4-ethylphenyl) arsine dihydroxide, $(C_2H_5.C_6H_4)_3As(OH)_2$, melts at 180°.[833]

Phenyldi(2,4-dimethylphenyl) arsine dihydroxide,

$$\begin{array}{lll} & C_6H_5 & \\ & \quad\diagdown & \\ & & As(OH)_2, \\ & \quad /\!/ & \\ [(CH_3)_2C_6H_3]_2 & & \end{array}$$

is obtained by the action of alkalis upon the corresponding halides, and melts at 112°. When heated it loses a molecule of water and is converted into the arsine *oxide,* m. p. 120°. Both the oxide and dihydroxide, when boiled with dilute nitric acid, yield a basic nitrate,

$$C_6H_5(C_8H_9)_2As.OH.NO_3,$$

consisting of transparent crystals, m. p. 126°.[1337]

Tri(2,4-dimethylphenyl) arsine dihydroxide, $[(CH_3)_2C_6H_3]_3As(OH)_2$, results from the interaction of the dibromide and alkali. On warming at 100° it loses water, yielding colorless crystals of the arsine *oxide.*[1338]

Phenyldi(2,4,5-trimethylphenyl) arsine dihydroxide,

$$\begin{array}{lll} [(CH_3)_3C_6H_2]_2 & & \\ & \diagdown\!\diagdown & \\ & & As(OH)_2, \\ & \quad / & \\ & C_6H_5 & \end{array}$$

is prepared by adding a slight excess of alcoholic potash to an alcoholic solution of any of the corresponding halides, saturating with carbon

On extracting the residue with alcohol and removing the solvent, the arsine dihydroxide crystallizes out in transparent, colorless prisms, m. p. 113-4°. When dehydrated either by prolonged standing in an evacuated desiccator or, more rapidly, by heating at 100°, it is converted into the corresponding arsine *oxide*, m. p. 162.5°, which is soluble in alcohol or benzene but sparingly so in ether.[1339]

Tri(2,4,5-trimethylphenyl)arsine dihydroxide,

$$[(CH_3)_3C_6H_2]_3As(OH)_2,$$

is made by hydrolyzing the corresponding dibromide or hydroxybromide with alcoholic potash, and crystallizes from dilute alcohol with four molecules of water. It effloresces in the air or, better, over sulfuric acid, while at 120° it is converted into the corresponding arsine *oxide*, m. p. 227-8°.[1340]

Tri(2,4,6-trimethylphenyl)arsine oxide is prepared from its halogen derivatives by the action of alcoholic potash. It is a white, crystalline powder, m. p. 203-4°.[1341]

Tri(4-isopropylphenyl)arsine oxide, $[(CH_3)_2CH.C_6H_4]_3AsO$, forms white needles, m. p. 129°, which on warming with dilute nitric acid yield a hydroxynitrate, colorless crystals, m. p. 147°; easily soluble in hot water or alcohol.[1320]

Tri(tertiary-butylphenyl)arsine oxide, $[(CH_3)_3C.C_6H_4]_3AsO$, m. p. above 360°, consists of a white, crystalline powder produced by treating the dichloride with water.[837]

Tri(4-phenylphenyl)arsine oxide, $(C_6H_5.C_6H_4)_3AsO$, from the corresponding dihalides and ammonia, melts at 264°.[1342]

Tri-α-naphthylarsine dihydroxide, $(C_{10}H_7)_3As(OH)_2$, is formed by adding alcoholic potash to the dibromide or hydroxybromide and precipitating with water,[1343] or by warming a carbon bisulfide solution of the arsine with sulfur monochloride, concentrating the solution, filtering and warming with dilute caustic potash.[838] The compound, m. p. above 300°, crystallizes from alcohol with two molecules of water as colorless needles. Drying the dihydroxide at 110° or boiling the hydroxybromide with water yields the corresponding arsine *oxide*, while hydrogen sulfide reduces the dihydroxide to the corresponding tertiary arsine.

Tri-β-naphthylarsine oxide, obtained by treating the impure tarry dibromide with alcoholic potash, crystallizes from alcoholic benzene in anhydrous needles.[1344]

Tricamphorylarsine dihydroxide, $\left[C_8H_{14}\begin{array}{l}\diagup CH \\ \\ \diagdown CO\end{array}\right]_3As(OH)_2$, is obtained as a by-product in the preparation of dicamphorylarsinic acid by condensing sodium camphor and arsenic trichloride in dry toluene. The reaction product is extracted with aqueous caustic soda, neutralized with mineral acid, and the resulting precipitate extracted with benzene, the insoluble residue consisting of the secondary acid. From the benzene extract more of the latter separates. The mother-liquor is then evaporated to dryness, the residue dissolved in dilute sodium hydroxide, boiled with charcoal, and the filtrate concentrated to crystallization. The crystals, consisting of sodium dicamphorylarsinate, are then removed, the filtrate acidified, and the viscid precipitate again treated with benzene and sodium hydroxide to remove the last traces of the secondary acid. The final precipitate is a brown, uncrystallizable solid softening at 110°, melting indefinitely at 130°, and easily soluble in benzene, alcohol or acetic acid. Its sodium salt is very soluble, while the silver salt is a grayish-white precipitate. When the dihydroxide is heated with an excess of aqueous caustic soda at 130-40° it decomposes into camphor and arsenic acid.[1345]

Tri(3-nitrophenyl)arsine oxide, $(O_2N.C_6H_4)_3AsO$, is prepared by introducing into a well-cooled mixture of fuming nitric and concentrated sulfuric acids either triphenylarsine,[841] or its dihydroxide.[1346] In the latter case the red, tarry matter, which is simultaneously formed, is removed by boiling alcohol, and the arsine oxide purified by recrystallization from hot glacial acetic acid. When pure it consists of colorless crystals, m. p. 254°; easily soluble in glacial acetic acid, insoluble in alcohol or ether, and exploding when strongly heated.

Tri(4-nitrophenyl)arsine oxide or *dihydroxide,* obtained by treating a solution of sodium di(4-nitrophenyl)arsenite with sodium 4-nitroisodiazobenzene at 75-80°, exists as brown crystals soluble in glacial acetic acid or alkali, insoluble in water, alcohol or aqueous sodium carbonate, and intumescing on heating.[776]

Tri(3-nitro-4-methylphenyl)arsine oxide, $\left(\begin{array}{l}O_2N\diagdown \\ \qquad\quad C_6H_3 \\ CH_3\diagup\end{array}\right)_3AsO$, is made by introducing tri(4-methylphenyl)arsine into a cooled mixture of fuming nitric and concentrated sulfuric acids, and crystallizes from alcohol in yellow, highly refractive, monoclinic prisms, m. p. 212°;

easily soluble in glacial acetic acid or hot alcohol, sparingly in cold alcohol and insoluble in ether. If, however, fuming sulfuric acid is used and the mixture kept warm, the product obtained is a nitrate, $[(O_2N)(CH_3)C_6H_3]_3As(NO_3)_2$, which crystallizes from glacial acetic acid in practically white crystals melting at 265°, and almost insoluble in alcohol. By heating with aqueous caustic potash it is converted into the corresponding oxide.[1347]

Tri(3-nitro-4-ethylphenyl)arsine oxide, $\left[\begin{array}{lr} O_2N & \\ & \diagdown C_6H_3 \\ C_2H_5 & \diagup \end{array}\right]_3 AsO$, melts at 232°.[833]

Trinitro-phenyldi(2,4-dimethylphenyl)arsine oxide,

$$\begin{array}{ll} [(O_2N)(CH_3)_2C_6H_2]_2 & \\ & \diagdown\!\diagdown AsO, \\ O_2N.C_6H_4 & \diagup \end{array}$$

results upon nitrating phenyldi(2,4-dimethylphenyl)arsine, and separates from alcohol as pale yellow crystals, m. p. 245°.[1337]

Trinitro-phenyldi(2,4,5-trimethylphenyl)arsine oxide,

$$(O_2N.C_6H_4)\left[\begin{array}{lr} O_2N & \\ & \diagdown C_6H \\ (CH_3)_3 & /\!/\!/ \end{array}\right]_2 AsO,$$

similarly prepared, crystallizes from alcohol in pale yellow crusts, m. p. 163°.[1348]

Tri(3-nitro-4-isopropylphenyl)arsine oxide, $\left[\begin{array}{lr} O_2N & \\ & \diagdown C_6H_3 \\ (CH_3)_2CH & \diagup \end{array}\right]_3 AsO$, yellowish-white needles from hot alcohol, melts at 245° with decomposition.[1349]

Tri(?-chloro-3-nitrophenyl)arsine oxide, $(O_2N.Cl.C_6H_3)_3AsO$.—From the corresponding dichloride by treatment with concentrated caustic potash solution. It is a white, crystalline mass, m. p. 257°; difficultly soluble in alcohol.[1350]

Tri(?-aminophenyl)arsine oxide, $(H_2N.C_6H_4)_3AsO$.—A mixture of arsenic trichloride and aniline in either dry benzene or toluene solution

is boiled for 50 hours and allowed to stand for three to eight weeks out of contact with atmospheric moisture, when the reaction product is rendered alkaline with sodium carbonate, and the excess aniline removed by distillation with steam. The hard, resinous residue upon repeated crystallization from benzene first yields an unidentified crystalline compound, m. p. 189°, the tri(aminophenyl)arsine oxide being obtained from the benzene mother liquors by concentrating and purifying through the hydrochloride. It is an amorphous, hygroscopic mass decomposing indefinitely at 108°. Its trihydrochloride is very soluble in water, and is precipitated as a gray, amorphous mass by passing hydrogen chloride into a benzene solution of the base. The platinichloride, $2(NH_2.4C_6H_4)_3AsO.3H_2PtCl_6$, is an amorphous, yellow substance sparingly soluble in water but insoluble in hydrochloric acid. The *triacetyl-* and *tribenzoylamino derivatives* melt at 140-50° and 130-40° respectively.[1351]

Tri(4-dimethylaminophenyl)arsine dihydroxide,

$$[(CH_3)_2N.C_6H_4]_3As(OH)_2.$$

A carbon bisulfide solution of the corresponding arsine is refluxed with sulfur monochloride for one hour, the intermediate product filtered off, dissolved in hydrochloric acid to remove the sulfur, and the dihydroxide precipitated from the filtrate by means of aqueous caustic potash. Recrystallized from ethyl acetate, it forms cubes, m. p. 257°; insoluble in water, very difficultly soluble in benzene, ether or carbon bisulfide and difficultly in methyl or ethyl alcohol.

The corresponding arsine *oxide* results on drying the preceding dihydroxide in vacuo at 100° to constant weight and then recrystallizing from alcohol. It consists of white crystals, m. p. 277°; easily soluble in methyl or ethyl alcohol, difficultly in ethyl acetate, very difficultly in ether or benzene and insoluble in water.[1352]

Tri(?-sulfophenyl)arsine oxide, $(HO_3S.C_6H_4)_3AsO$.—Triphenylarsine is first converted into its dihydroxide by heating on a water-bath with concentrated sulfuric acid and precipitating with aqueous caustic potash, and then sulfonated by further heating with concentrated sulfuric acid to the boiling point of the latter. The compound is isolated as the barium salt, a white, crystalline powder easily soluble in water.[1353]

4-Carboxyphenyldiphenylarsine oxide, [Diphenyl-p-benzarsonic acid],

$$\begin{array}{l} (C_6H_5)_2 \\ \qquad\quad \diagdown \\ \qquad\qquad AsO, \\ \qquad\quad \diagup \\ HOOC.C_6H_4 \end{array}$$

is derived from diphenyl-4-methylphenylarsine either by heating with nitric acid (d, 1.2) in a sealed tube, or by oxidation with potassium permanganate for 4-5 weeks at 60°. It crystallizes from alcohol in crusts, m. p. 253-4°; easily soluble in alcohol, alkalis or excess of mineral acids but insoluble in water or ether. With hydrogen sulfide in alcoholic solution it yields the corresponding arsine sulfide, while with hydrogen chloride in the same solvent it forms the ethyl ester of 4-carboxytriphenylarsine dichloride.

The silver salt, a pulverulent precipitate sensitive to light, is prepared by treating an aqueous suspension of the acid with moist silver oxide and concentrating the filtrate. The acid barium salt is a white powder easily soluble in water.[1354]

4-Carboxy-4′-methyltriphenylarsine oxide [*Phenyl-p-tolyl-p-benzarsonic acid*],

$$\begin{array}{l} C_6H_5 \diagdown \\ C_7H_7 - AsO. \\ HOOC.C_6H_4 \diagup \end{array}$$

—When phenyldi(4-methylphenyl)arsine is oxidized with potassium permanganate at 50-60° for three weeks, it yields a mixture of the mono- and dicarboxylic acids, which are separated by means of cold absolute alcohol, the monocarboxylic acid alone dissolving. The latter is insoluble in water, ether or benzene, and does not melt below 300°. Its silver salt forms needles which turn brown on exposure to air.[1355]

4,4′-Dicarboxytriphenylarsine oxide [*Phenyldi-p-benzarsonic acid*],

$$\begin{array}{l} C_6H_5 \diagdown \\ \quad AsO. \\ (HOOC.C_6H_4)_2 /\!\!/ \end{array}$$

A suspension of phenyldi(4-methylphenyl)arsine in water containing caustic potash is allowed to react with potassium permanganate for eight weeks at 50-60°, the whole being shaken vigorously from time to time. The desired product is isolated by filtering the reaction-mixture, concentrating the filtrate, and finally precipitating with hydrochloric acid. The compound crystallizes from hot glacial acetic acid as a white, crystalline powder soluble in hot alcohol or alkalis, insoluble in water, ether or chloroform, and remaining unmelted below 300°. It is a dibasic acid, forming a white, microcrystalline silver salt, a blue, pulverulent copper salt which loses its one molecule of water of crystallization at 105°, and an acid barium salt consisting of white crystals easily soluble in water.[1356]

Bis(carboxytolyl)phenylarsine oxide, $\begin{array}{l} \quad\quad\quad\quad\quad C_6H_5 \\ \quad\quad\quad\quad\quad\quad\quad \diagdown \\ \quad\quad\quad\quad\quad\quad\quad\quad AsO, \\ \quad\quad\quad\quad\quad\quad\quad /\!/ \\ [HOOC.C_6H_3(CH_3)]_2 \end{array}$ is

a dibasic compound formed on heating phenyldi(2,4-dimethylphenyl)-arsine with a calculated amount of nitric acid (d, 1.2) in a sealed tube at 110-70°. It crystallizes from alcohol as a pale yellow powder, m. p. 196°; sparingly soluble in water.[828]

Bis(carboxyxylyl)phenylarsine oxide, $\begin{array}{l} \quad\quad\quad\quad\quad\quad C_6H_5 \\ \quad\quad\quad\quad\quad\quad\quad\quad \diagdown \\ \quad\quad\quad\quad\quad\quad\quad\quad\quad AsO, \\ \quad\quad\quad\quad\quad\quad\quad\quad /\!/ \\ [HOOC.C_6H_2(CH_3)_2]_2 \end{array}$

is derived from phenyldi(2,4,5-trimethylphenyl)arsine (2 g.) and 4.7 g. of nitric acid (d, 1.2) by heating in a sealed tube for 12 hours at 120-80°, and is purified by repeatedly dissolving in ammonia and reprecipitating with hydrochloric acid. It crystallizes from hot dilute alcohol as a pale yellow powder, m. p. 199°; insoluble in water, ether or benzene.[1357]

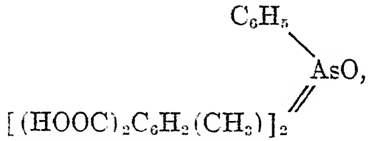
Tri(4-carboxyphenyl)arsine dihydroxide, [*Tri-p-benzarsonic acid*], $(HOOC.C_6H_4)_3As(OH)_2$, is prepared by oxidizing tri(4-methylphenyl)-arsine with alkaline potassium permanganate, and may be recrystallized from ether in granular crystals somewhat soluble in water or hydrochloric acid. When heated it loses water without melting. Its alkali and alkali earth salts indicate that the acid is tribasic, the silver salt alone containing four atoms of the metallic element. The potassium salt forms crystalline crusts easily soluble in water; the calcium derivative is a flocculent precipitate containing 1-2 molecules of water, while the silver salt appears to have the formula,

$$(AgOOC.C_6H_4)_3As.OH.OAg.$$ [1358]

2,4,2′,4′-Tetracarboxytriphenylarsine oxide, $\begin{array}{l} \quad\quad\quad\quad\quad C_6H_5 \\ \quad\quad\quad\quad\quad\quad\quad \diagdown \\ \quad\quad\quad\quad\quad\quad\quad\quad AsO, \\ \quad\quad\quad\quad\quad\quad\quad /\!/ \\ [(HOOC)_2C_6H_3]_2 \end{array}$

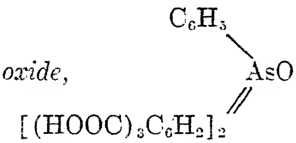
is a tetrabasic acid obtained upon oxidizing phenyldi(2,4-dimethylphenyl)arsine with the calculated amount of nitric acid (d, 1.2) in a sealed tube at 110-70°. Recrystallized from alcohol it melts at 213°, and is fairly easily soluble in hot water or alcohol.[828]

Bis(dicarboxytolyl)phenylarsine oxide,

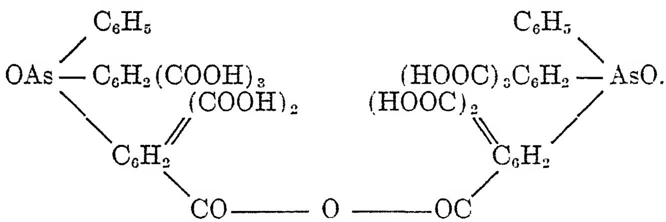


m. p. 213°, is made like the corresponding dicarboxytetramethyl derivative, using twice the amount of nitric acid.[1357]

Bis(tricarboxyphenyl)phenylarsine oxide,



is prepared like the preceding compound employing the proper quantity of nitric acid and heating for 13 hours at 110-50°. It crystallizes from dilute alcohol as hard, white crystals, m. p. 275°. The composition of the silver salt and the ethyl ester suggest the existence of an anhydride having the formula,



The silver salt, a white powder sensitive to light, is obtained by the addition of silver nitrate to a solution of the ammonium salt, while the ethyl ester, silky needles, m. p. 193°, results on saturating an alcoholic solution of the acid with hydrogen chloride, allowing to evaporate in vacuo and finally recrystallizing from hot alcohol. The ester contains no chlorine and is soluble in dilute alkali only on prolonged warming.[1359]

3. *Triarylarsine Sulfides.*—The addition of sulfur and triaryl arsines may be readily effected either in the presence of a suitable solvent such as carbon bisulfide, or by fusion. The same products are obtained from the above arsines either by treatment with yellow ammonium sulfide in alcoholic solution, or by first combining with sulfur monochloride, and then decomposing the addition products with hydrogen sulfide:

$$R_3As + S_2Cl_2 \longrightarrow R_3As\begin{matrix} Cl \\ S.S.Cl \end{matrix} \xrightarrow{H_2S} R_3AsS + 2HCl + S_2.$$

They also result upon boiling triarylarsine dihalides with yellow ammonium sulfide, or when hydrogen sulfide acts upon alcoholic solutions of triarylarsine dihalides, hydroxyhalides, dihydroxides or oxides.

The products are crystalline solids generally soluble in hot, but less so in cold alcohol and insoluble in alkali sulfides. The nuclear substituted compounds also possess properties characteristic of the particular substituents present.

Triphenylarsine sulfide, $(C_6H_5)_3AsS$, is made by boiling the dichloride with yellow ammonium sulfide; by prolonged boiling of the arsine and sulfur in carbon bisulfide solution, or by fusing triphenylarsine with sulfur.[1360] A very efficient method of preparation consists in passing hydrogen sulfide through an alcoholic solution of triphenylarsine dihydroxide,[1333] while the same product results on refluxing a carbon bisulfide solution of the arsine with sulfur monochloride on a water-bath for one hour, introducing hydrogen sulfide until fumes of hydrogen chloride are no longer evolved, and evaporating off the solvent.[854] In each case the crude product is recrystallized from hot alcohol, forming lustrous needles, m. p. 162°; difficultly soluble in cold alcohol and insoluble in water, acids, ether or alkali sulfides.

Tri(3-methylphenyl)arsine sulfide, $(CH_3.C_6H_4)_3AsS$, silvery needles, m. p. 186°, is obtained like the para isomer, avoiding an excess of sulfur.[1307]

Diphenyl-4-methylphenylarsine sulfide, $(C_6H_5)_2(CH_3.C_6H_4)AsS$, results on passing hydrogen sulfide through an alcoholic solution of the dihydroxide. It separates from alcohol as white, granular crystals, m. p. 135°.[1361]

Phenyldi(4-methylphenyl)arsine sulfide, $C_6H_5(CH_3.C_6H_4)_2AsS$, m. p. 144°, is similarly produced from the corresponding arsine oxide.[1362]

Tri(4-methylphenyl)arsine sulfide, $(C_7H_7)_3AsS$, may be obtained by saturating an aqueous solution of the hydroxychloride with hydrogen sulfide, or by warming the tertiary arsine with sulfur in carbon bisulfide solution. It crystallizes from dilute alcohol as lustrous leaflets, m. p. 170-1°.[1363]

Tribenzylarsine sulfide, $(C_6H_5.CH_2)_3AsS$.—From the arsine oxide by passing hydrogen sulfide into its alcoholic solution, or by warming the components together in glacial acetic acid. It crystallizes in colorless, transparent, rhombic prisms, m. p. 212-14°; sparingly soluble in hot chloroform or glacial acetic acid and insoluble in alcohol, ether, benzene, carbon disulfide or acetone.[1364]

Tri(4-ethylphenyl)arsine sulfide, $(C_2H_5.C_6H_4)_3AsS$, melts at 123°.[833]

Phenyldi(2,4-dimethylphenyl)arsine sulfide, $C_6H_5[(CH_3)_2C_6H_3]_2AsS$, can only be obtained with difficulty.[820]

Tri(2,4-dimethylphenyl)arsine sulfide, $[(CH_3)_2C_6H_3]_3AsS$, silky prisms melting at 145°, is made by the interaction of its components.[1338]

Phenyldi(2,4,5-trimethylphenyl)arsine sulfide,

$$C_6H_5[(CH_3)_3C_6H_2]_2AsS,$$

is prepared by heating the arsine with alcoholic yellow ammonium sulfide in a sealed tube at 110°. From alcohol or alcohol-ether mixture it crystallizes as transparent crystals, m. p. 135°.[1348]

Tri(4-isopropylphenyl)arsine sulfide, $[(CH_3)_2CH.C_6H_4]_3AsS$, from the corresponding arsine oxide by passing hydrogen sulfide through its alcoholic solution, separates from hot alcohol as white crystals, m. p. 149.5°.[1349]

Tri(4-phenylphenyl)arsine sulfide, $(C_6H_5.C_6H_4)_3AsS$, melts at 228°, and is prepared by passing hydrogen sulfide through an alcoholic solution of the corresponding arsine oxide, dihalide or hydroxyhalide. It may be recrystallized from benzene.[1342]

Tri-α-naphthylarsine sulfide, $(C_{10}H_7)_3AsS$.—Tri-α-naphthylarsine in carbon bisulfide solution is warmed on a water-bath with sulfur monochloride, treated with ammonium pentasulfide, and again warmed for some time. After filtering off the unchanged pentasulfide, the desired compound is obtained by concentrating the filtrate. It crystallizes from alcohol in small, white plates, m. p. 285°; easily soluble in chloroform or ethyl acetate, difficultly in benzene or carbon bisulfide and insoluble in water.[1365]

Tri-β-naphthylarsine sulfide is prepared by passing hydrogen sulfide through a dilute alcoholic solution of the dibromide, forming well-defined tablets, m. p. 162°; readily soluble in benzene or carbon bisulfide but sparingly in ether or alcohol. By refluxing its benzene solution with mercury the sulfur is removed, mercuric sulfide and the free arsine being obtained.[1344]

Tri(3-amino-4-methylphenyl)arsine sulfide, $(H_2N.C_6H_3CH_3)_3AsS$.—An alcoholic solution of the tertiary amino arsine is saturated first with ammonia, then with hydrogen sulfide, and finally refluxed for some time. Upon standing the sulfide settles out together with sulfur, and is purified by treating with hot alcohol and carbon bisulfide. The compound is soluble in most dilute acids but insoluble in all organic solvents. With dilute sulfuric acid the acid sulfate,

$$2(NH_2.C_6H_3.CH_3)_3AsS.3H_2SO_4,$$

is obtained as a white precipitate easily soluble in hot dilute hydrochloric acid but insoluble in water.[850]

Tri(4-dimethylaminophenyl)arsine sulfide, $[(CH_3)_2N.C_6H_4]_3AsS$.—The corresponding arsine in carbon bisulfide solution is first refluxed with sulfur monochloride and then with an excess of finely powdered ammonium pentasulfide, after which the precipitated reaction-product is dissolved in hydrochloric acid, the sulfur filtered off, and the crude arsine sulfide reprecipitated with sodium carbonate. By dissolving in chloroform and reprecipitating with absolute alcohol, the compound is obtained in the form of lustrous leaflets, m. p. 269-70°; difficultly soluble in carbon bisulfide, benzene, ether or alcohol but easily in chloroform.[1352]

4-Carboxyphenyldiethylarsine sulfide, $(C_2H_5)_2(HOOC.C_6H_4)AsS$, formed on passing hydrogen sulfide into an aqueous solution of the hydroxychloride crystallizes in long, colorless, transparent needles, m. p. 184°.[1366]

4-Carboxytriphenylarsine sulfide, $(C_6H_5)_2(HOOC.C_6H_4)AsS$, separates as oily drops on passing hydrogen sulfide through an alcoholic solution of the arsine and evaporating off the solvent. On standing the oily substance solidifies to a mass of beautiful white crystals, m. p. 178°.[823]

D. Quaternary Derivatives.

1. *Arsonium Compounds*.—Tertiary aromatic arsines combine with alkyl or aryl halides to form quaternary arsenicals of the type R_4AsX, where X represents a halogen atom:

$$R_3As + R'X \longrightarrow R_4AsX.$$

This reaction often occurs at ordinary or slightly elevated temperatures, but in several instances it has been found necessary to heat the components together in a sealed tube at water-bath or even higher temperatures, depending upon the nature of the individual arsine and alkyl or aryl halide employed. Thus, combination with methyl iodide takes place very readily, while with ethyl iodide and the halides of the higher homologues the reaction is not only more difficult, but in several instances does not take place at all.

Instead of tertiary arsines, cacodyls may be employed, in which case a secondary halogenated arsine is also formed. The reaction evidently proceeds according to the following equation:

$$R_2As.AsR_2 + R'X \longrightarrow \underset{\dot{X}}{R_2As}\!-\!\underset{\dot{R}'}{AsR_2} \longrightarrow R_2R'As + R_2AsX \xrightarrow{R'X}$$

$$R_2R'_2AsX + R_2AsX.$$

Quaternary halides are also obtainable from primary aromatic arsines and alkyl halides:

$$RAsH_2 + 3R'X \longrightarrow RR'_3AsX + 2HX;$$

from arsonium hydroxides and haloid acids:

$$R_4As.OH + HX \longrightarrow R_4AsX + H_2O;$$

or by heating arseno compounds in a sealed tube with an alkyl iodide. According to Bertheim the latter reaction proceeds as follows:

$$RAs = AsR + 3R'I \longrightarrow RR'_3AsI + RAsI_2,$$

while Steinkopf claims that the arsonium triiodide is first formed, and this in turn reacts with the unchanged arseno compound, yielding an arsonium iodide and an aryl diiodoarsine:

$$\begin{cases} RAs = AsR + 6R'I \longrightarrow 2RR'_3AsI_3 \\ RAs = AsR + 2RR'_3AsI_3 \longrightarrow 2RR'_3AsI + 2RAsI_2. \end{cases}$$

The last reaction can be actually carried out by bringing together arsenobenzene and phenyltrimethylarsonium triiodide in alcoholic solution.

The iodides and bromides are well-defined crystalline compounds, while the chlorides either crystallize poorly or exist as syrupy masses which form crystalline addition products with platinic, mercuric or auric chloride. The arsonium halides are all generally soluble in water or alcohols but not in ether. Some of the iodides combine additively with chlorine to form dichloroiodides, others yield double salts with cadmium-, lead- or mercuric iodide, and still others form triiodides with iodine, but they all possess the property of yielding the corresponding arsonium chloride when boiled with silver chloride. The bromides are converted into the iodides by heating with methyl or potassium iodide.

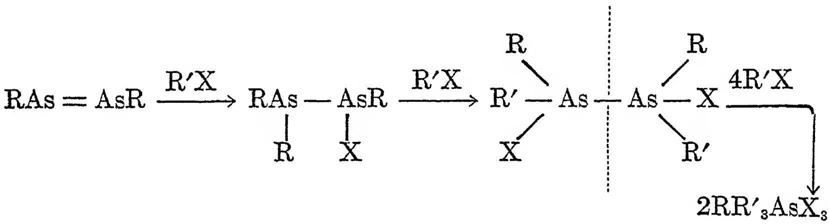
When heated at elevated temperatures in an atmosphere of carbon dioxide, the arsonium halides generally split into their component tertiary arsines and alkyl or aryl halides. They react with silver d-α-bromocamphor-π-sulfonate, yielding silver halide and the corresponding

arsonium bromocamphorsulfonate, while with freshly prepared moist silver oxide they form the corresponding arsonium hydroxides. The latter are strong bases readily forming salts with acids—even with so weak an acid as carbonic, which they rapidly absorb upon exposure to air.

It is interesting to note that arsonium compounds with an assymetric arsenic atom have been prepared, and there appears to exist definite evidence that they may be resolved into optically active components, but the active compounds racemize so rapidly that the observed rotation is small. This racemization appears to occur as a result of the tendency of the quaternary salt to readily dissociate in solution. The arsonium salts of optically active acids, however, exhibit a molecular rotation which is practically equal to that of the acid ion itself.

The arsonium triiodides are prepared:

1. From arseno compounds by heating with an excess of alkyl iodide in a sealed tube:



2. In a similar manner from alkyl iodides and secondary monohalogenated-, cyano- or thiocyanoarsines, or tertiary arsine dihalides:

$$R_2AsX \xrightarrow{R'X} R_2R'AsX_2 \xrightarrow{RX} R_2R'_2AsX_3.$$

3. By adding iodine to an arsonium iodide in a solvent such as alcohol:

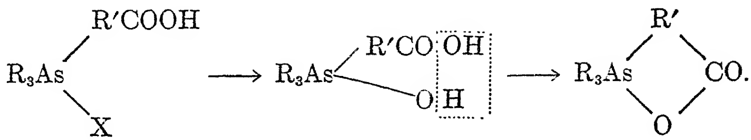
$$R_4AsI + I_2 \longrightarrow R_4AsI_3.$$

As we have already seen under the preparation of arsonium iodides, the triiodides give up their extra halogen to arseno compounds, converting the latter into two molecules of the corresponding diiodoarsines, while they themselves are changed to the arsonium iodides. In the case of diphenyldimethylarsonium triiodide, it has been found possible to effect combination with still more iodine, forming an enneaiodide, $R_4AsI.I_8$, a compound closely resembling the corresponding derivatives in the nitrogen series.

Arsonium compounds containing carboxy groups may be prepared by oxidizing the nuclear alkyl radicals of arylarsonium compounds by means of potassium permanganate; from carboxylated tertiary arsines and alkyl halides; or from tertiary arsines and halogenated fatty acids such as chloroacetic acid:

$$R_3As + ClCH_2.COOH \longrightarrow R_3As\begin{matrix} \diagup Cl \\ \diagdown CH_2COOH \end{matrix} .$$

The above arsonium halides form addition products with platinic or auric chloride, but with alkalis the corresponding hydroxides or their inner anhydrides are obtained:

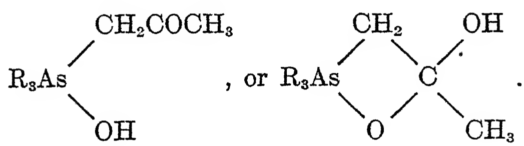


The latter are basic compounds which yield arsonium salts upon treatment with acids. The anhydrides, unlike the corresponding phosphorus compounds, are very stable toward concentrated caustic alkalis, decomposition occurring only on prolonged boiling in alcoholic potassium hydroxide solution.

Tertiary arsines also combine additively with ω-halogenated ketones according to the equation:

$$R_3As + ClCH_2COCH_3 \longrightarrow R_3As\begin{matrix} \diagup CH_2COCH_3 \\ \diagdown Cl \end{matrix}$$

The resulting halides, upon treatment with sodium carbonate, are converted into the corresponding hydroxides, known as arseniketobetaines. The latter form salts with acids but, unlike the other arsonium hydroxides, are readily crystallizable, only slightly soluble in water and neutral in reaction. It has not been definitely determined whether they possess the structural formula



In the case of triphenylmethylarseniketobetaine, it has been found possible by heating to form an anhydride which yields the parent substance upon treatment with hydrous solvents.

Phenyltrimethylarsonium chloride, $C_6H_5(CH_3)_3AsCl$, is obtained from the corresponding iodide by treating with silver oxide and adding hydrochloric acid to the resulting compound. Its platinichloride,

$$[C_6H_5(CH_3)_3As]_2PtCl_6,$$

crystallizes in beautiful, red lamellæ melting at 219° and readily soluble in water.[1367]

Phenyltrimethylarsonium bromide results from the interaction of methyl bromide and either phenyldimethylarsine [768] or symm. dimethyldiphenyldiarsine [1368] in a sealed tube. It separates from alcohol in compact crystals, m. p. 284° with decomposition; soluble in water, methyl or ethyl alcohol, difficultly in warm acetone, chloroform, benzene or ethyl acetate and insoluble in ether or pyridine. Its platinichloride crystallizes in brown leaflets, m. p. 197-200°. With picric acid the arsonium bromide yields the corresponding picrate,

$$C_6H_5(CH_3)_3As.OC_6H_2(NO_2)_3,$$

orange-yellow needles melting at 145°.

Phenyltrimethylarsonium iodide may be obtained from phenyldimethylarsine [1369] or arsenobenzene [1370] by warming in a sealed tube with methyl iodide; from symm. dimethyldiphenyldiarsine and methyl iodide in an atmosphere of carbon dioxide; [571] from the corresponding bromide by heating with methyl iodide; [205] or from phenylarsine by heating with an excess of methyl iodide.[1371] It crystallizes in white needles, m. p. 244-50°; is easily soluble in cold water or alcohol, insoluble in ether, and decomposes into its constituents upon heating in a stream of carbon dioxide. With cadmium iodide it forms a double salt,

$$[C_6H_5(CH_3)_3As]_2.CdI_4,$$

a white, crystalline precipitate melting at 194°.[1372] With iodoform in absolute alcoholic solution the arsonium iodide forms an addition product, $I[(C_6H_5)(CH_3)_3As]....I_3CH$, which can also be obtained by refluxing a mixture of either iodoform, phenyldimethylarsine and methyl iodide, or phenyltrimethylarsonium hydroxide and iodoform. It crystallizes in yellow needles, m. p. 143-5°; soluble in acetone or hot alcohol, difficultly in ether, pyridine or chloroform, and is decomposed into its components on boiling with water.[1373]

Phenyltrimethylarsonium triiodide.—From phenylmethylchloro- or iodoarsine and methyl iodide in a sealed tube for two hours at 100°. On digesting the reaction product with ether and recrystallizing from alcohol, it forms long brown needles, m. p. 103°; easily soluble in hot alcohol or cold acetone, sparingly in cold alcohol and insoluble in water, ether or ligroin.[733] On refluxing its alcoholic solution with symm. diphenyldiiododiarsine, the resulting compounds are largely phenyldiiodoarsine and phenyltrimethylarsonium iodide: [577]

$$\left(\begin{matrix}C_6H_5\\I\end{matrix}>As\right)_2 + C_6H_5(CH_3)_3AsI_3 \longrightarrow 2C_6H_5AsI_2 + C_6H_5(CH_3)_3AsI.$$

4-Methoxyphenyltrimethylarsonium iodide, $(CH_3O.C_6H_4)(CH_3)_3AsI$, is obtained along with 4-methoxyphenyldiiodoarsine upon heating 4,4′-dimethoxyarsenobenzene with methyl iodide in a sealed tube at 100°. It forms beautiful, long, white needles and prisms, m. p. 213°; soluble in water, methyl alcohol, glacial acetic acid, chloroform or pyridine, less so in acetone and insoluble in ether, ligroin or benzene.[492]

4-Iodophenyltrimethylarsonium iodide, $(I.C_6H_4)(CH_3)_3AsI$, from 4,4′-diiodoarsenobenzene and methyl iodide, crystallizes in leaflets or prisms melting at about 300°, soluble in water, methyl alcohol or glacial acetic acid, less so in acetone, sparingly in chloroform and insoluble in ether or ligroin.[1374]

4-Carboxyphenyltrimethylarsonium chloride [*Trimethylarseniben-zobetaine hydrochloride*], $\begin{array}{l}(CH_3)_3 \diagdown\!\!\!\diagdown\!\!\!\diagdown \\ \qquad\qquad AsCl \\ HOOC.C_6H_4 \diagup\end{array}$, prepared by the prolonged oxidation of 4-methylphenyltrimethylarsonium chloride with alkaline potassium permanganate at 50°, crystallizes from water in clusters of small white needles easily soluble in hot, but less so in cold alcohol and decomposing above 400° into phenyltrimethylarsonium chloride and carbon dioxide. Its platinichloride exists as small, pale yellow needles, m. p. 255°, while the aurichloride consists of golden-yellow needles, m. p. 198°.

The *free betaine,* $(CH_3)_3As\begin{array}{c}\diagup\; C_6H_4 \;\diagdown \\ \diagdown\;\; O \;\;\diagup\end{array}CO$, results upon treating the above arsonium chloride with sodium carbonate, and crystallizes from dilute alcohol in thin plates containing 2½ molecules of water of crystallization. Heating decomposes it without melting; treatment with hydrobromic acid yields the arsonium bromide, small needles decomposing without melting at 270°; aqueous nitric acid produces a nitrate, leaflets melting at 230°, while with sulfuric acid long, thin needles of an acid sulfate are produced. When boiled with alcoholic potash the betaine decomposes into trimethylarsine oxide and benzoic acid.[1375]

Phenyldimethylethylarsonium iodide, $(C_6H_5)(CH_3)_2(C_2H_5)AsI$, is made by reacting either phenyldimethylarsine and ethyl iodide,[791] or phenylmethylethylarsine and methyl iodide.[797] It crystallizes from alcohol as colorless needles, m. p. 142°. With mercuric iodide in acetone solution it combines additively, forming pale yellow prisms of

$(C_6H_5)(CH_3)_2(C_2H_5)As.HgI_3$, m. p. 135°, while with lead iodide the compound $(C_6H_5)(CH_3)_2(C_2H_5)As.PbI_3$, m. p. 203°, is obtained.[1372]

Phenylmethyldiethylarsonium chloride, $(C_6H_5)(CH_3)(C_2H_5)_2AsCl$, is an oil which forms a crystalline double salt, m. p. 190°, with platinic chloride.[1277] The arsonium *iodide* is readily prepared by combining phenyldiethylarsine with methyl iodide at ordinary temperature. It separates from alcohol-ether as prisms, m. p. 122° (M.) 75-7° (B.).[793, 1376]

4-Carboxyphenylmethyldiethylarsonium iodide,

$$\begin{array}{l} CH_3\diagdown \\ (C_2H_5)_2 = AsI, \\ HOOC.C_6H_4\diagup \end{array}$$

consists of white needles turning pale yellow on exposure to sunlight and melting at 131°. It is produced by refluxing the tertiary arsine with methyl iodide on a water-bath.[1377]

Phenyliodomethyldiethylarsonium iodide, $\begin{array}{l} ICH_2\diagdown \\ (C_2H_5)_2 = AsI, \\ C_6H_5\diagup \end{array}$ separates on warming phenyldiethylarsine with methylene iodide on a water-bath and finally cooling. It crystallizes from dilute alcohol as small needles, m. p. 173°; difficultly soluble in hot water, alcohol or acetone, more readily in methyl alcohol.[1378]

Phenylcarboxymethyldiethylarsonium chloride [*Phenyldiethylarsenibetaine hydrochloride*], $\begin{array}{l} C_6H_5\diagdown \\ (C_2H_5)_2 = AsCl, \\ HOOC.CH_2\diagup \end{array}$ results on combining phenyldiethylarsine with monochloroacetic acid at water-bath temperature. It crystallizes in white needles, m. p. 125°; is easily soluble in alcohol or water, and forms a lustrous, red, crystalline platinichloride melting at 161°. The *free betaine* results on adding alcoholic potash to a similar solution of the above hydrochloride, removing the excess alkali with carbon dioxide and concentrating the filtrate. The ethyl ester of the hydrochloride is an oil obtained by heating phenyldiethylarsine together with ethyl chloroacetate in a sealed tube at 100°, and extracting with ether. Its chloroplatinate crystallizes from alcohol in small needles melting at 125°, while the picrate melts at 90°.[1379]

Phenyltriethylarsonium chloride, $C_6H_5(C_2H_5)_3AsCl$, may be derived directly from the corresponding iodide either by boiling with freshly precipitated silver chloride, or indirectly by heating with an aqueous suspension of silver oxide for several hours in a sealed tube at 110°, neutralizing the resulting hydroxide with hydrochloric acid, and evaporating the solution on the water-bath. It is a syrupy mass which cannot be obtained crystalline. With platinic chloride its aqueous solution yields a double salt consisting of golden-yellow leaflets.[1380]

Phenyltriethylarsonium iodide results upon heating either phenyldiethylarsine and ethyl iodide in a sealed tube at 100°,[1381] or phenylarsine and an excess of ethyl iodide in a sealed tube at 120°.[1371] It crystallizes in colorless prisms, m. p. 112-3°; soluble in water or alcohol, insoluble in ether, and having an extremely bitter taste. On exposure to sunlight it acquires a yellow color due to the liberation of iodine, while heating in a current of carbon dioxide splits it into phenyldiethylarsine and ethyl iodide. When chlorine is conducted into its glacial acetic acid solution, a dark oil separates which soon solidifies to lustrous, dark yellow crystals of the arsonium *dichloroiodide*, $C_6H_5(C_2H_5)_3As.ICl_2$.[1376]

Phenyltriethylarsonium hydroxide is obtained by treating the corresponding arsonium halides with moist silver oxide.[1382]

4-Carboxyphenyltriethylarsonium chloride [*Triethylarsenibenzobetaine hydrochloride*],

$$\begin{array}{l} (C_2H_5)_3 \diagdown \\ \qquad\qquad\quad AsCl, \\ HOOC.C_6H_4 \diagup \end{array}$$

prepared like the corresponding methyl derivative, consists of hygroscopic acicular crystals, which are decomposed into triethylarsine oxide and benzoic acid only after prolonged boiling with alcoholic caustic potash:

$$(HOOC.C_6H_4)(C_2H_5)_3AsCl + 2KOH \longrightarrow$$
$$(C_2H_5)_3AsO + C_6H_5COOK + KCl + H_2O.$$

The chloroplatinate forms small, pale yellow leaflets, m. p. 225°; its aurichloride crystallizes from alcohol in thin, yellow leaflets and from hot water containing hydrochloric acid in long, thin, golden-yellow needles, m. p. 165°, while the picrate,

$$[(HOOC.C_6H_4)(C_2H_5)_3]As.OC_6H_2(NO_2)_3,$$

is obtained as golden-yellow leaflets, m. p. 155°.

The *free betaine*, derived from its hydrochloride by treatment with an excess of sodium carbonate, separates as long, tabular, hygroscopic crystals having a bitter taste. It forms no salts with alkalis.[1383]

Phenylethyl-n-propylallylarsonium bromide, $\begin{array}{l} C_6H_5 \\ C_2H_5 - AsBr, \\ C_3H_7 \\ C_3H_5 \end{array}$ results when phenylethyl-n-propylarsine and allyl bromide interact for 24 hours. It crystallizes from acetone in large, colorless plates, m. p. 86°; moderately soluble in water. The corresponding *d-α-bromocamphor-π-sulfonate* crystallizes readily from dilute alcohol, and melts at 123°.[796]

Phenyltriisoamylarsonium iodide, $C_6H_5(C_5H_{11})_3AsI$, from isoamyl iodide and phenylarsine, exists as white crystals, m. p. 163°; soluble in alcohol or chloroform but insoluble in cold water, ether, benzene or ligroin.[1371]

4-Methylphenyltrimethylarsonium iodide, $\begin{array}{r} (CH_3)_3 \\ AsI, \\ (CH_3.C_6H_4) \end{array}$ may be prepared either from 4-methylphenyldimethylarsine and methyl iodide,[453] or by heating arseno-p-toluene together with methyl iodide in a sealed tube for one hour at 100°.[1374] It crystallizes from water as broad, flat plates or needles, m. p. 247.5°; soluble in water, glacial acetic acid, methyl or ethyl alcohol, difficultly so in acetone or chloroform and insoluble in ether or ligroin. With platinic chloride it forms a double salt consisting of reddish-yellow needles, m. p. 225°.

4-Methylphenylmethyldiethylarsonium iodide,

$$(CH_3.C_6H_4)(CH_3)(C_2H_5)_2AsI,$$

colorless leaflets, m. p. 220°, from 4-methylphenyldiethylarsine and methyl iodide.[798]

4-Methylphenyltriethylarsonium iodide, $\begin{array}{r} (C_2H_5)_3 \\ AsI, \\ (CH_3.C_6H_4) \end{array}$ is obtained from 4-methylphenyldiethylarsine and ethyl iodide as colorless prisms melting at 230°, and possessing a bitter taste. The corresponding arsonium *hydroxide* results on treating the iodide with moist silver oxide. On neutralizing a solution of the hydroxide with hydrochloric acid, the arsonium *chloride* separates as an oil which upon standing gradually solidifies to a crystalline solid. The latter forms with platinic chloride a double salt consisting of reddish-yellow leaflets, m. p. 210°; soluble in alcohol or hot water.[798]

γ-Phenylpropyltrimethylarsonium iodide,

$$(C_6H_5.CH_2CH_2CH_2)(CH_3)_3AsI,$$

prepared from γ-phenylpropyldimethylarsine and methyl iodide, crystallizes from water in colorless needles melting at 144°.[265]

α-Naphthyltrimethylarsonium iodide, $C_{10}H_7(CH_3)_3AsI$, is readily formed from its components, crystallizing from alcohol in colorless needles, m. p. 230°.[794]

α-Naphthyldimethylethylarsonium iodide,

$$\begin{array}{l} (CH_3)_2 \diagdown \\ C_2H_5 - AsI, \\ C_{10}H_7 \diagup \end{array}$$

produced by condensing α-naphthyldimethylarsine with ethyl iodide at 90-100°, crystallizes from alcohol in colorless leaflets, m. p. 218°.[794]

Diphenyldimethylarsonium iodide,

$$\begin{array}{l} (C_6H_5)_2 \diagdown \\ \qquad AsI. \\ (CH_3)_2 \diagup \end{array}$$

—Methyl iodide reacts vigorously with diphenylmethylarsine at ordinary temperature, forming the corresponding arsonium iodide, which may be best crystallized from dilute alkalis as white, spicular crystals, m. p. 190°; easily soluble in alcohol or hot water, less so in cold water, insoluble in ether, and having a bitter taste. When heated in a stream of carbon dioxide, it is split into its components; warming with moist silver oxide produces the arsonium *hydroxide,* which upon neutralization with hydrochloric acid yields the corresponding *chloride.* The latter forms with platinic chloride a double salt crystallizing from hot water in flattened, reddish-yellow needles, m. p. 219° with decomposition, and sparingly soluble in cold water.[1384]

Diphenyldimethylarsonium triiodide results upon heating diphenylchloro-, bromo- or iodoarsine with methyl iodide in a sealed tube for several hours at 100°, and consists of violet needles, m. p. 69.5°; easily soluble in chloroform, ethyl acetate, acetone or hot methyl or ethyl alcohol, sparingly in the cold alcohols and insoluble in water or ether.[747, 750]

Diphenyldimethylarsonium enneaiodide,

$$\begin{array}{l} (C_6H_5)_2 \diagdown \\ \qquad AsI.I_8. \\ (CH_8)_2 \diagup \end{array}$$

—When the

preceding triiodide and iodine are dissolved in a saturated alcoholic iodine solution by warming, and the whole allowed to cool, the ennea-iodide separates as lustrous, metallic, dark green needles which have a strong odor of iodine, readily turn brown on warming, and melt at 56°.[1385] Its excess iodine may be easily split off.

Diphenylmethylethylarsonium iodide, $\begin{array}{l} CH_3 \diagdown \\ C_2H_5 - AsI \\ (C_6H_5)_2 \diagup\!\!\diagup \end{array}$, is best formed by heating either ethyl iodide and diphenylmethylarsine or methyl iodide and diphenylethylarsine in a sealed tube at water-bath temperature. It may be crystallized from weakly alkaline solutions, or by dissolving in alcohol and precipitating with ether, as white needles or rhombic prisms sensitive to light, m. p. 170°; easily soluble in hot water, slightly in cold, insoluble in ether, and having a very bitter taste. When warmed in a current of carbon dioxide, it dissociates into diphenylmethylarsine and ethyl iodide.

Upon warming the compound with moist silver oxide, it yields the corresponding arsonium *hydroxide,* a syrupy liquid which absorbs carbon dioxide from the air, has an intensely bitter taste and a strongly alkaline reaction. When neutralized with dilute hydrochloric acid the arsonium *chloride* is formed. This in turn combines with platinic chloride to form a double salt crystallizing from hot water in yellowish-red to red needles, m. p. 214° with decomposition; difficultly soluble in cold water and insoluble in alcohol. Upon warming the above hydroxide with a solution of picric acid, the arsonium picrate,

$$\begin{array}{l} CH_3 \diagdown \\ C_2H_5 - As.OC_6H_2(NO_2)_3, \\ (C_6H_5)_2 \diagup\!\!\diagup \end{array}$$

separates on cooling as a resinous mass which after recrystallization from hot alcohol yields yellow needles. It is soluble in hot water, difficultly in cold, insoluble in ether, and melts at 95°, above which temperature it decomposes.[1386]

Diphenyldiethylarsonium chloride, $\begin{array}{l} (C_2H_5)_2 \diagdown\!\!\diagdown \\ \qquad AsCl \\ (C_6H_5)_2 \diagup\!\!\diagup \end{array}$.—From the corresponding iodide by heating with moist silver oxide in a sealed tube for 2-3 hours at 110°, and subsequently neutralizing with dilute hydrochloric acid. With platinic chloride it forms a golden-yellow product which crystallizes in platelets difficultly soluble in water.

Diphenyldiethylarsonium iodide results upon heating diphenylethylarsine or its dichloride with ethyl iodide in a sealed tube at 100°. It crystallizes from hot water as white, flattened needles, m. p. 184°; difficultly soluble in cold water, readily in alcohol, and is somewhat sensitive to light.[1387]

Phenyl-4-methylphenylmethylethylarsonium iodide,

$$\begin{array}{l} CH_3 \diagdown \\ \quad C_2H_5 - AsI, \\ \quad C_6H_5 \diagup \\ CH_3.C_6H_4 \diagup \end{array}$$

results from the interaction of the tertiary arsine and methyl iodide. It crystallizes in white, monoclinic, acicular needles, m. p. 150-1° (from water) and 145° (from alcohol). It is noteworthy because it contains five different radicals attached to the arsenic, so that stereoisomeric forms are theoretically possible. Although its alcoholic solution shows a slight optical activity, it has not been found possible to resolve it into optically active isomerides by means of tartaric or aspartic acid. Moreover, fission fungi could not be employed as the arsenical has a toxic action upon them. The striking difference in the melting points of the crystals obtained from water and from alcohol is due to the fact that each consists of a mixture of various stereoisomers. The corresponding arsonium *chloride* obtained by the action of hydrochloric acid upon the hydroxide, is not crystallizable, but its platinichloride crystallizes from hot water in yellowish-red, triclinic prisms, m. p. 214°.[809]

Phenyl-4-methylphenyldiethylarsonium iodide, $\begin{array}{l} (C_2H_5)_2 \diagdown\!\!\diagdown \\ \quad C_6H_5 - AsI, \\ CH_3.C_6H_4 \diagup \end{array}$

separates from water as monoclinic prisms, m. p. 148°.[1388]

Phenyl-4-methylphenylethyl-n-propyl- and *isopropylarsonium iodides,* $(C_6H_5)(C_7H_7)(C_2H_5)(C_3H_7)AsI$, consist of monoclinic crystals with no sharp melting points.[1388]

Phenylbenzyldimethylarsonium iodide, $\begin{array}{l} (CH_3)_2 \diagdown\!\!\diagdown \\ \quad C_6H_5 - AsI, \\ C_6H_5.CH_2 \diagup \end{array}$ is readily produced by combining additively phenyldimethylarsine and benzyl iodide. It crystallizes from a mixture of acetone and ether in colorless needles, m. p. 115-6°.[791]

Phenyl-ω-chlorobenzyldimethylarsonium chloride,

$$(C_6H_5)(C_6H_5.CHCl)(CH_3)_2AsCl,$$

is made by heating phenyldimethylarsine with an excess of benzal chloride, and precipitating the product with ether. It is a deliquescent substance whose -ω-chlorine is replaced by a hydroxyl on dissolving in water. The *hydroxy compound* forms a double salt with platinic chloride.[1389]

Phenylbenzylmethylallylarsonium iodide,

$$(C_6H_5)(C_6H_5.CH_2)(CH_3)(C_3H_5)AsI.$$

On allowing a mixture of phenylmethylallylarsine and benzyl iodide to stand for several days, a hygroscopic, vitreous mass is formed which, after repeated recrystallizations from acetone, separates as large, colorless crystals, m. p. 100°; readily soluble in acetone, alcohol or ethyl acetate but insoluble in water. It reacts with silver d-α-bromocamphor-π-sulfonate under ordinary conditions to form the corresponding arsonium *bromocamphorsulfonate,* which crystallizes from a mixture of alcohol and acetone in large, colorless prisms, m. p. 189°.[802]

Phenyl-α-naphthylmethylallylarsonium bromide,

$$(C_6H_5)(C_{10}H_7)(CH_3)(C_3H_5)AsBr,$$

is easily made by combining the tertiary arsine with allyl bromide, and forms a colorless crystalline compound melting with decomposition at 140°.[1390]

Phenyl-α-naphthylphenacylmethylarsonium bromide,

$$\left.\begin{array}{r} CH_3 \\ C_6H_5 \\ C_{10}H_7 \\ C_6H_5COCH_2 \end{array}\right\rangle AsBr.$$

When phenyl-α-naphthylmethylarsine and ω-bromoacetophenone are warmed together in molecular proportions, a glassy substance is produced which in contact with warm alcohol slowly changes to a bulky, white, crystalline solid, m. p. 189°. It is sparingly soluble in cold, readily in hot alcohol and insoluble in acetone. The corresponding *bromocamphorsulfonate* has been obtained as a glassy mass which resisted repeated attempts at crystallization.[1390]

Phenyl-α-naphthylhomopiperonylmethylarsonium bromide,

$$\left.\begin{array}{r} CH_3 \\ C_5H_5 \\ C_{10}H_7 \\ C_8H_7O_2 \end{array}\right\rangle AsBr,$$

is readily formed upon warming together equimolecular quantities of homopiperonyl bromide and phenyl-α-naphthylmethylarsine. The compound crystallizes from alcohol in colorless plates, m. p. 174-5°. Its *bromocamphorsulfonate* crystallizes from absolute alcohol in needles containing alcohol of crystallization.[1350]

Phenylbenzylethyl-n-propylarsonium iodide,

$$(C_6H_5)(C_7H_7)(C_2H_5)(C_3H_7)AsI,$$

from molecular proportions of phenylethyl-n-propylarsine and benzyl iodide at 40-50° for two hours, crystallizes from ethyl acetate in small, colorless crystals, m. p. 128°; soluble in alcohol but not in water. With silver d-camphor-β-sulfonate silver iodide is precipitated, the corresponding arsonium *camphorsulfonate* remaining in solution. The latter may be isolated by evaporating the solution, and crystallizing the residue from a mixture of acetone and light petroleum.[803]

Phenyl-γ-phenylpropyldimethylarsonium iodide,

$$(C_6H_5)(C_6H_5.CH_2CH_2CH_2)(CH_3)_2AsI,$$

is readily prepared from phenyl-γ-phenylpropylmethylarsine and methyl iodide, crystallizing from water as colorless rhombohedra, m. p. 102°.[801]

Phenyl-α-naphthyldimethylarsonium iodide, $\begin{array}{l} (CH_3)_2 \diagdown\!\!\diagdown \\ C_6H_5 - AsI, \\ C_{10}H_7 \diagup \end{array}$ similarly prepared from the arsine and methyl iodide at water-bath temperature, separates from a concentrated alcoholic solution as colorless plates, m. p. 175°.[806]

Di(2-methylphenyl)dimethylarsonium iodide, $\begin{array}{l} (CH_3)_2 \diagdown\!\!\diagdown \\ \qquad\qquad AsI, \\ (CH_3.C_6H_4)_2 \diagup\!\!\diagup \end{array}$ is readily obtained from di(2-methylphenyl)methylarsine and methyl iodide, crystallizing from water as colorless needles, m. p. 195°.[805]

Triphenylmethylarsonium iodide, $(C_6H_5)_3(CH_3)AsI$, prepared by refluxing triphenylarsine with methyl iodide on a water-bath, crystallizes from alcohol as yellowish leaflets and from water as colorless, feathery needles, m. p. 176°; easily soluble in alcohol or ether, less so in hot water and insoluble in cold water. By conducting chlorine into its glacial acetic acid solution, or by treating with sodium hypochlorite and hydrochloric acid the *dichloroiodide,* $(C_6H_5)_3(CH_3)AsI.Cl_2$, is ob-

tained. The same compound results on adding iodine chloride solution to the corresponding arsonium chloride, and crystallizes in yellow leaflets, m. p. 144°; easily soluble in boiling alcohol, acetone or glacial acetic acid but insoluble in water or ether. By repeated evaporation with water the iodine is volatilized, leaving the corresponding arsonium *chloride.*[1391] The latter is also obtained by neutralizing a solution of the hydroxide with hydrochloric acid or by boiling the solution of the arsonium iodide with silver chloride. Upon concentrating its solution a thick syrup is obtained which, after several evaporations with water, is finally dissolved in alcohol and reprecipitated with ether, yielding white needles, m. p. 121°; soluble in water and alcohol. With platinic chloride it forms a double salt crystallizing from alcoholic hydrochloric acid in yellowish-red needles, m. p. 224-5°.[1392]

Triphenylmethylarsonium triiodide is obtained from triphenylarsine diiodide and methyl iodide by heating for three hours in a sealed tube at 100°, or from the arsonium iodide and iodine in alcoholic solution. It crystallizes from alcohol in lustrous, brown leaflets, m. p. 107°; easily soluble in acetone or boiling alcohol, difficultly in carbon bisulfide or cold alcohol and insoluble in water, ether, carbon tetrachloride or petroleum ether.[767]

Triphenylmethylarsonium bromide, from triphenylarsine and methyl bromide in a sealed tube at room temperature for 14 days, melts at 195°; is insoluble in ether, benzene or ligroin, slightly soluble in acetone or water and readily in methyl or ethyl alcohol, hot water or chloroform. With iodoform in hot absolute alcoholic solution it forms an addition compound, $Br[(C_6H_5)_3(CH_3)As]\ldots I_3CH$, brownish-yellow laminæ, m. p. 124°; slightly soluble in warm ether, acetone, benzene, toluene or ligroin, readily in hot alcohol or chloroform, and is decomposed into its components on boiling with water.[1393]

Triphenylmethylarsonium hydroxide is best made by digesting an alcoholic solution of the iodide with moist silver oxide, and carefully concentrating the resulting solution by keeping it in vacuo over sulfuric acid. It consists of elongated, transparent, prismatic crystals soluble in water with an alkaline reaction, and melting at 125-6°. When heated at 100°, the compound loses methyl alcohol, leaving pure triphenylarsine. Its aqueous solution absorbs carbon dioxide from the air, and on evaporation deposits large plates of the bicarbonate,

$$[(C_6H_5)_3(CH_3)As.HCO_3].H_2O,$$

which effervesces with acids, forms a white precipitate with baryta water, and slightly reddens phenolphthalein in the cold, though more so on boiling. By adding an excess of nitric acid to a solution of the hydroxide

and concentrating, there is obtained a crystalline mass of the nitrate, which may be recrystallized from alcohol-ether in long needles.[1392]

Tri(3-nitrophenyl)methylarsonium nitrate,

$$(O_2N.C_6H_4)_3(CH_3)AsNO_3,$$

is produced by treating either triphenylmethylarsonium nitrate or chloride with a mixture of fuming nitric and concentrated sulfuric acids at low temperature. The product is a yellow powder, m. p. 195°; soluble in hot alcohol, chloroform or glacial acetic acid, insoluble in water, and intumescing when heated.[1394]

Triphenyliodomethylarsonium iodide, $(C_6H_5)_3(ICH_2)AsI$, produced upon heating triphenylarsine and methylene iodide in an oil bath at 130°, crystallizes from hot dilute alcohol as silvery needles, m. p. 227°; sparingly soluble in glacial acetic acid, chloroform or water and insoluble in anhydrous ether. By passing chlorine into its hot glacial acetic acid solution the corresponding *chloromethylarsonium dichloroiodide,*

$$(C_6H_5)_3(CH_2Cl)As.ICl_2,$$

is obtained as intensely yellow crystals, m. p. 138°; readily soluble in boiling alcohol, sparingly in cold alcohol or glacial acetic acid. Upon warming with caustic soda solution it is decomposed into triphenylarsine dihydroxide and dichloroiodomethane:

$$\begin{cases} (C_6H_5)_3(CH_2Cl)As.ICl_2 + 2NaOH \longrightarrow \\ \qquad\qquad (C_6H_5)_3(CH_2Cl)AsI + NaClO + NaCl + H_2O \\ (C_6H_5)_3(CH_2Cl)As.ICl_2 + NaClO + NaOH \longrightarrow \\ \qquad\qquad (C_6H_5)_3As(OH)_2 + CHICl_2 + 2NaCl. \end{cases}$$

When an alcoholic solution of the iodomethylarsonium iodide is warmed with freshly precipitated silver chloride the corresponding arsonium *chloride* is obtained as lustrous needles, m. p. 208°; easily soluble in alcohol or water.[1395]

Triphenylhydroxymethylarsonium chloride, $(HO.CH_2)(C_6H_5)_3AsCl$.—By shaking a solution of the corresponding iodomethylarsonium iodide with silver oxide, both iodine atoms are replaced by hydroxyls, and the product is obtained as a syrup on concentrating. However, by first adding hydrochloric acid and then concentrating, the hydroxymethylarsonium chloride is obtained as a deliquescent, crystalline solid, m. p.

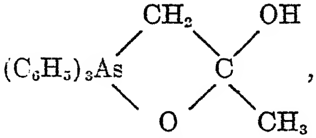
112°. With platinic chloride in alcoholic solution it forms a double salt consisting of lustrous needles, m. p. 224°.

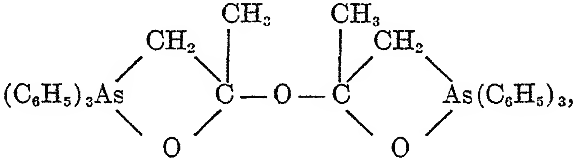
If hydriodic acid is employed in the above neutralization, the corresponding hydroxymethylarsonium *iodide* is formed along with some triphenylarsine which is removed with ether. The iodide crystallizes from alcohol as flat, yellow needles, m. p. 171°; easily soluble in water or alcohol.[1396]

Triphenyl-β-hydroxyethylarsonium chloride [*Triphenylarsinocholine chloride*], $(C_6H_5)_3(HOCH_2.CH_2)AsCl$, is derived from triphenylarsine by prolonged boiling with ethylene chlorhydrin. It is first precipitated by ether and then recrystallized from alcohol-ether as colorless needles, m. p. 215°. With platinic chloride it forms a double salt consisting of elongated golden-yellow needles, m. p. 223°.[1397]

Triphenylcarboxymethylarsonium chloride [*Triphenylarsenibetaine hydrochloride*], $\begin{array}{l} (C_6H_5)_3 \diagdown\!\!\diagdown\!\!\diagdown \\ \qquad\qquad AsCl \\ HOOC.CH_2 \diagup \end{array}$, is obtained as white needles, m. p. 145°, and easily soluble in water or alcohol when equimolecular quantities of triphenylarsine and chloroacetic acid are heated together on a water-bath. It forms a light red platinichloride, m. p. 194°. With alcoholic caustic potash it yields the corresponding arsonium *hydroxide*—small, white needles, m. p. 125°; very easily soluble in water or alcohol. At 100° the latter loses one molecule of water, forming an inner anhydride, *triphenylarsenibetaine*, $(C_6H_5)_3As\begin{array}{c} \diagup CH_2 \diagdown \\ \diagdown\ O\ \diagup \end{array}CO$.[1398]

Triphenylacetonylarsonium chloride [*Triphenylmethylarseniketobetaine hydrochloride*], $\begin{array}{l} (C_6H_5)_3 \diagdown\!\!\diagdown\!\!\diagdown \\ \qquad\qquad\quad AsCl \\ CH_3COCH_2 \diagup \end{array}$.—From triphenylarsine and chloroacetone by heating for several hours in an oil-bath at 120°. It crystallizes from alcohol-ether as rectangular crystals, m. p. 172°; easily soluble in water or alcohol. Its platinichloride is a reddish-brown precipitate soluble in alcoholic hydrochloric acid.

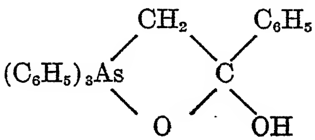
The *free ketobetaine,*  , results upon adding caustic soda or sodium carbonate solution to the hydrochloride and recrystallizing from hot water, forming nacreous, rhombic plates practically insoluble in cold water, sparingly in ether and readily in hot water, alcohol or benzene. The compound melts at 123°, then resolidifies and remelts at 194°. This is due to the fact that the betaine gradually loses one-half molecule of water, forming the anhydride,



which melts at the higher temperature. The anhydride may be recrystallized unchanged from benzene, but in hydrated solvents it reverts to the ketobetaine. By adding various acids to the alcoholic solution of the ketobetaine and subsequently precipitating with ether, salts may be obtained.

Triphenylacetonylarsonium bromide, prepared from the ketobetaine and hydrobromic acid, forms colorless crystals melting at 165°, and dissolving in water or alcohol. The *iodide,* m. p. 161°, is readily soluble in alcohol or hot water but sparingly in cold water.[1399]

Triphenylphenacylarsonium bromide [*Tetraphenylarseniketobetaine hydrobromide*], $(C_6H_5)_3(CH_2COC_6H_5)AsBr$, results upon heating equal parts of triphenylarsine and bromoacetophenone on a water-bath. It forms silky needles, m. p. 178°; easily soluble in hot water or alcohol but sparingly in cold water. The corresponding *chloride* is soluble in water or alcohol and melts at 166°; the platinichloride melts at 191°, while the *iodide,* prepared by adding a solution of potassium iodide to a hot solution of the bromide, melts at 157°, is easily soluble in alcohol, and sparingly in cold water. The nitrate, from the chloride or bromide and silver nitrate, consists of colorless needles, m. p. 184°; soluble in alcohol, sparingly in cold water. Upon treating the bromide with sodium hydroxide or carbonate, there is formed *tetraphenylarseniketobetaine,*

 ,

which may be crystallized from dilute alcohol in fine, white needles, m. p. 176°; readily soluble in alcohol but insoluble in cold water.[1400]

Triphenylethylarsonium iodide, $(C_6H_5)_3(C_2H_5)AsI$, results on refluxing triphenylarsine with ethyl iodide. It may be recrystallized from alcohol-ether as lustrous needles, m. p. 158°; difficultly soluble in water but readily in alcohol. The corresponding *chloride* forms a platinichloride melting at 221°.[1401]

Tri(2-methylphenyl)methylarsonium iodide, $(CH_3.C_6H_4)_3(CH_3)AsI$, crystallizes from water in colorless needles, m. p. 166°.[811]

Tri(3-methylphenyl)methylarsonium iodide, easily prepared by the interaction of the tertiary arsine and methyl iodide at ordinary temperature, crystallizes from water or alcohol in rhombic prisms, m. p. 181°. The corresponding arsonium *chloride* is oily, but its platinichloride is a pale yellow precipitate. On warming the arsonium iodide with alkali, tri(3-methylphenyl)arsine is obtained.[1307]

Tri(3-methylphenyl)ethylarsonium iodide, $(C_7H_7)_3(C_2H_5)AsI$, crystallizes from dilute alcohol in distorted rhombohedra of the triclinic system, m. p. 130°.[1402]

Diphenyl-4-methylphenylmethylarsonium iodide,

$$(C_6H_5)_2(CH_3.C_6H_4)(CH_3)AsI,$$

obtained like triphenylmethylarsonium iodide, crystallizes from water in white needles, m. p. 152°. The corresponding *chloride* is oily and cannot be obtained crystalline, but the platinichloride crystallizes from alcoholic hydrochloric acid in pale red crystals, m. p. 209°.[1361]

Diphenyl-4-methylphenylethylarsonium iodide,

$$(C_6H_5)_2(C_7H_7)(C_2H_5)AsI,$$

is an oil which cannot be solidified. The platinichloride forms pink crystals, m. p. 220°.[1354]

Phenyldi(4-methylphenyl)methylarsonium iodide,

$$(C_6H_5)(C_7H_7)_2(CH_3)AsI,$$

made like triphenylmethylarsonium iodide, crystallizes from water in white needles, m. p. 84°, which turn pale yellow on exposure to light. Its platinichloride crystallizes from hot dilute hydrochloric acid in lustrous, golden-yellow needles, m. p. 222°.[1403]

Phenyldi(4-methylphenyl)ethylarsonium iodide,

$$(C_6H_5)(C_7H_7)_2(C_2H_5)AsI,$$

is an oily substance which solidifies very slowly to form small yellowish crystals, m. p. 125°.[1356]

Tri(4-methylphenyl)methylarsonium iodide,

$$(CH_3.C_6H_4)_3(CH_3)AsI,$$

is prepared like its phenyl homologue, and melts at 179°; the *chloride* forms large, transparent crystals, m. p. 87°, while the platinichloride consists of strongly refractive, reddish-brown prisms. By passing chlorine into a glacial acetic acid solution of the iodide, there is obtained the *dichloroiodide*, $(C_7H_7)_3(CH_3)As.ICl_2$, which on recrystallization from alcohol separates as reddish-yellow crystals, m. p. 146°.[1363]

Tri(3-dimethylamino-4-methylphenyl)methylarsonium iodide,

$$[C_6H_3(CH_3)N(CH_3)_2]_3(CH_3)AsI.$$

Tri(3-amino-4-methylphenyl)arsine is refluxed with an excess of methyl iodide, the excess of the latter distilled off, the reddish-yellow, crystalline residue dissolved in water, and the desired compound precipitated with caustic soda as a white powder, m. p. 135°; easily soluble in alcohol but sparingly in water.[852]

Tri(4-methylphenyl)iodomethylarsonium iodide, $(ICH_2)(CH_3.C_6H_4)_3AsI$,

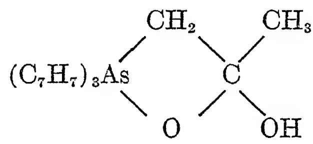
prepared as above, consists of colorless crystals melting at 215°, and dissolving in alcohol.[1363]

Tri(4-methylphenyl)carboxymethylarsonium chloride [*Tri-p-tolylarsenibetaine hydrochloride*], $(CH_3.C_6H_4)_3(HOOCCH_2)AsCl$, is prepared as above,

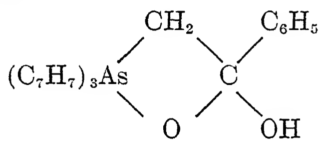
but the combination occurs less readily. It is a white, crystalline mass, m. p. 146°, which forms a yellow platinichloride, m. p. 206°. The *free betaine* crystallizes less readily than the corresponding phenyl compound so that it cannot be obtained absolutely pure.[1404]

Tri(4-methylphenyl)acetonylarsonium chloride [*Tri-p-tolylmethylarseniketobetaine hydrochloride*], $(C_7H_7)_3(CH_3COCH_2)AsCl$.—Prepared by heating molecular proportions of chloroacetone and tri(4-methylphenyl)arsine in sealed tubes at 85°. It melts at 170°, and is readily soluble in water or alcohol but insoluble in ether. It forms a platini-

chloride, consisting of yellow leaflets, m. p. 210°; sparingly soluble in water or alcohol. The arsonium *bromide,* obtained from the chloride and potassium bromide, exists as needles, m. p. 159°; easily soluble in alcohol, less so in water. The corresponding *iodide* melts at 144°.

The *free ketobetaine,*  , is obtained by the action of alkali upon the chloride, and crystallizes from dilute alcohol in lustrous needles, m. p. 113°; easily soluble in alcohol, benzene or ether but insoluble in water.[1405]

Tri(4-methylphenyl)phenacylarsonium chloride [*Tri-p-tolylphenylarseniketobetaine hydrochloride*], $(C_7H_7)_3(C_6H_5COCH_2)AsCl$, is prepared as above by employing chloroacetophenone, and is recrystallized from alcohol-ether as white needles, m. p. 159°, which behave with solvents like the preceding chloride. Its platinichloride forms yellowish-red needles, m. p. 205°. The *bromide,* also derived as above, melts at 182°, and the *iodide* at 148°.

The *free ketobetaine,*  , crystallizes from alcohol containing a little water in tufts of lustrous needles melting at 160°.[1406]

Tri(4-methylphenyl)ethylarsonium iodide crystallizes from water in fine, colorless needles, m. p. 158°.[1363]

Diphenylbenzylmethylarsonium iodide,

$$(C_6H_5)_2(C_6H_5.CH_2)(CH_3)AsI,$$

from diphenylmethylarsine and benzyl iodide, melts at 193°.[794]

Phenyl-4-methylphenylbenzylethylarsonium iodide,

$$(C_6H_5)(C_7H_7)(C_6H_5.CH_2)(C_2H_5)AsI,$$

from phenyl-4-methylphenylethylarsine and benzyl iodide, forms rhombic crystals, m. p. 150°. The corresponding *chloride* is uncrystallizable.[754]

Phenylbenzyl-α-naphthylmethylarsonium bromide,

$$\begin{array}{l} \qquad\quad CH_3 \\ \qquad\qquad\quad \diagdown \\ \qquad\quad C_6H_5 - AsBr. \\ \qquad\qquad\quad \diagup \\ C_6H_5.CH_2 \diagup \\ \qquad C_{10}H_7 \end{array}$$

Phenyl-α-naphthylmethylarsine and benzyl bromide combine readily when heated on a water-bath, to form the arsonium bromide. It crystallizes in colorless prisms, m. p. 185°; readily soluble in cold dilute or hot absolute alcohol, sparingly in cold absolute alcohol and insoluble in water. With a calculated quantity of silver d-α-bromocamphor-π-sulfonate it forms the arsonium *bromocamphorsulfonate* which separates from acetone, alcohol-ethyl acetate or acetone-ether as colorless prisms, m. p. 187°; soluble in aqueous acetone or alcohol and almost insoluble in water. Its rotating power is $[M]_D 281°$, which may be raised to 300° by recrystallization.[1407]

d-Phenylbenzyl-α-naphthylmethylarsonium bromide is prepared like the iodide as colorless crystals, m. p. 187-8°, but racemization in solution is very rapid, the highest molecular rotation observed being $[M]_D + 5°$. The corresponding arsonium *iodide* is obtained when d-phenylbenzyl-α-naphthylmethylarsonium-d-α-bromocamphor-π-sulfonate in aqueous acetone is treated with aqueous potassium iodide, separating in colorless needles, m. p. 186-7°, having a molecular rotation of $[M]_D 12°$. It is soluble in cold chloroform or a mixture of alcohol and water, and in warm alcohol or acetone. The last two solutions deposit an inactive iodide, m. p. 183-4°, upon cooling.[1408]

Tribenzylalkylarsonium iodides are prepared by heating the arsine with a slight excess of alkyl iodides in sealed tubes at 100°. They are crystalline compounds readily soluble in alcohol or hot water, the solubilities decreasing with increasing carbon content, while the solubilities in ether increase in the same order. They have an intensely bitter taste, turn yellowish in the air, and have melting points varying within but few degrees of each other. In alcoholic solution silver nitrate precipitates silver iodide.[1409]

Tribenzylmethylarsonium iodide, $(C_6H_5.CH_2)_3(CH_3)AsI$, consists of colorless needles and rhombic crystals, m. p. 143°. Boiling with moist silver oxide converts it into the arsonium *hydroxide*—a highly caustic base which absorbs carbon dioxide from the air. However, on boiling the iodide with concentrated caustic potash, it decomposes with the formation of toluene. By neutralizing the hydroxide with hydrochloric

acid, the arsonium *chloride* is obtained as white needles, m. p. 201°; readily soluble in alcohol or hot water. Its aqueous solution combines with platinic chloride to form a yellow, double salt melting at 173°.[1410]

Tribenzylethylarsonium iodide, $(C_6H_5CH_2)_3(C_2H_5)AsI$, consists of white leaflets, m. p. 148°.[1411]

Tri(4-ethylphenyl)methylarsonium iodide, $(C_2H_5.C_6H_4)_3(CH_3)AsI$, from the arsine and methyl iodide, melts at 126°.[833]

Phenyldi(2,4-dimethylphenyl)methylarsonium iodide,

$$(C_6H_5)[(CH_3)_2C_6H_3]_2(CH_3)AsI,$$

obtained from phenyldi(2,4-dimethylphenyl)arsine and methyl iodide, consists of lustrous white crystals, m. p. 184°, while the corresponding arsonium *hydroxide* melts at 122°.[1337]

Phenyldi(2,4-dimethylphenyl)ethylarsonium iodide,

$$(C_6H_5)[(CH_3)_2.C_6H_3]_2(C_2H_5)AsI,$$

from the arsine and ethyl iodide, is a solid, m. p. 157°.[1337]

Tri(2,4-dimethylphenyl)methylarsonium iodide,

$$[(CH_3)_2C_6H_3]_3(CH_3)AsI,$$

forms large, lustrous crystals, m. p. 179°; sparingly soluble in water, easily in alcohol or chloroform; the *chloride* is an uncrystallizable, enamel-like mass, but its platinichloride consists of reddish-brown crystals, m. p. 245°.[1338]

Tri(2,5-dimethylphenyl)methylarsonium iodide exists as white, tabular crystals, m. p. 175°; the platinichloride as pale yellow needles, m. p. 250°. Warming the hydroxide splits it into the tertiary arsine and methyl alcohol.[831]

Phenyldi(2,4,5-trimethylphenyl)methylarsonium iodide,

$$C_6H_5[C_6H_2(CH_3)_3]_2CH_3AsI,$$

melts at 179°; the *chloride* at 192°, and the platinichloride at 266.5°, while the *hydroxide,* formed by treating the iodide in alcohol solution with moist silver oxide, exists as colorless needles, m. p. 151°, which on continued heating at 130° is split into methyl alcohol and the tertiary arsine.[1348]

Phenyldi(2,4,5-trimethylphenyl)ethylarsonium iodide,

$$(C_6H_5)[(CH_3)_3C_6H_2]_2(C_2H_5)AsI,$$

forms colorless crystals, m. p. 189°.[1348]

Tri(2,4,6-trimethylphenyl)methylarsonium iodide,

$$[(CH_3)_3C_6H_2]_3(CH_3)AsI,$$

is prepared from its components by warming together on a water-bath. It crystallizes from alcohol as yellowish-red prisms, but from hot water as white prisms, m. p. 186°; sparingly soluble in hot water and easily in alcohol or chloroform. The *chloride* separates from alcohol as tufts of crystals, m. p. 192°, readily soluble in alcohol or water, while its platinichloride forms yellowish-red monoclinic crystals, m. p. 237°.[1341]

Tri(4-isopropylphenyl)methylarsonium iodide,

$$[(CH_3)_2CH.C_6H_4]_3(CH_3)AsI,$$

forms white rosets, m. p. 103°.[1349]

Tri(4-isopropylphenyl)ethylarsonium iodide,

$$[(CH_3)_2CH.C_6H_4]_3(C_2H_5)AsI,$$

melts at 138°.[834]

Tri(tertiary-butylphenyl)methylarsonium iodide,

$$[(CH_3)_3C.C_6H_4]_3(CH_3)AsI,$$

consists of crystals, m. p. 125° with decomposition, while the *hydroxide,* m. p. 136°, crystallizes with four molecules of water which cannot be removed without decomposing the compound.[837]

Tri(4-phenylphenyl)methylarsonium iodide,

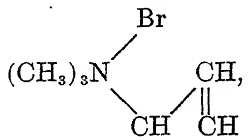
$$(C_6H_5.C_6H_4)_3(CH_3)AsI,$$

from the arsine and methyl iodide, crystallizes from benzene or alcohol in tufts of crystals, m. p. 155°; the corresponding *chloride* melts at 112°.[1412]

Tri(3-methylphenyl)-n-propylarsonium iodide, $(C_7H_7)_3(C_3H_7)AsI$, is prepared by the prolonged interaction of the tertiary arsine and n-propyl iodide at ordinary temperature. It crystallizes from dilute alcohol in needles, m. p. 143°.[1402] The *isopropyl* derivative melts at 162°.[830]

Tribenzyl-n-propylarsonium iodide, $(C_6H_5.CH_2)_3(C_3H_7)AsI$, forms colorless, monoclinic plates, m. p. 145-6°; the *isopropyl* derivative consists of colorless, tabular crystals, m. p. 143°,[1411] while the *isoamyl* compound, $(C_6H_5.CH_2)_3(C_5H_{11})AsI$, is obtained as colorless crystals, m. p. 146°.[1413]

Tri(4-methylphenyl)allylarsonium chloride, $(C_7H_7)_3(C_3H_5)AsCl$, is a yellow oil, but its platinichloride is a red powder, m. p. 225°. The corresponding *bromide,* formed by refluxing the arsine and allyl bromide on a water-bath for several hours, crystallizes from hot water as beautiful, white prisms, and from dilute alcohol as lustrous crystals, m. p. 82°; easily soluble in water, alcohol, chloroform and the other ordinary solvents except ether. With an excess of bromine in alcoholic solution a snow-like mass of tri(4-methylphenyl)-β, γ-dibromopropylarsonium bromide, $(C_7H_7)_3(CH_2Br.CHBr.CH_2)AsBr$, is obtained. It is soluble in hot water, alcohol or benzene and sparingly in cold water. With alcoholic potash it does not yield a compound similar to



but a viscid, uncrystallizable oil. By continued heating with water on a water-bath there is formed tri(4-methylphenyl)arsine, so that it seems to be a compound which is easily decomposed. At 120-30° it loses 1HBr, a brown, resinous, uncrystallizable mass remaining.

Tri(4-methylphenyl)allylarsonium iodide, made by treating the bromide with concentrated potassium iodide solution, crystallizes from aqueous alcohol in colorless prisms, m. p. 141°; easily soluble in alcohol but sparingly in cold water.[1414]

Tri(3-methylphenyl)benzylarsonium chloride,

$$(C_7H_7)_3(C_6H_5.CH_2)AsCl,$$

is prepared by the prolonged interaction of the arsine with benzyl chloride at 30-40°, forming well-defined crystals, m. p. 102°; easily soluble in alcohol, sparingly in water.[830]

Tetrabenzylarsonium chloride, $(C_6H_5.CH_2)_4AsCl$, is prepared by refluxing tribenzylarsine and benzyl chloride, or by heating the components in a sealed tube at 170-5° for three hours. It forms triclinic crystals containing one molecule of water of crystallization, melts at 160°, and dissolves in hot water or alcohol. Its aqueous solution yields a precipitate with nitric acid, picric acid, potassium bichromate, thiocyanate, bromide or iodide. The mercurichloride crystallizes in white needles difficultly soluble in water and melting at 176°; the platinichloride is a yellow, insoluble precipitate, m. p. 197-8°, while the aurichloride forms very small needles melting indefinitely at 130°.[1413, 1415]

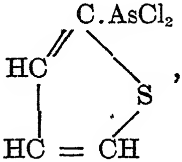
Tetrabenzylarsonium bromide is made either by the addition of potassium bromide to a concentrated solution of the preceding chloride

or by neutralizing the arsonium hydroxide with hydrobromic acid. It separates from hot water or alcohol as felted needles, m. p. 173°.[1416] The *iodide,* produced either like the bromide, or by refluxing tribenzylarsine oxide with red phosphorus and hydriodic acid, crystallizes from alcohol in transparent needles sparingly soluble in hot water and melting at 168°. Its crystalline mercuriiodide melts at 163°, is easily soluble in acetone but insoluble in water or ether.[1416, 1415] An arsonium *triiodide* is formed by the interaction of alcoholic solutions of the monoiodide and iodine, and crystallizes in lustrous, red leaflets, m. p. 149-50°. The arsonium *hydroxide* is obtained from the iodide and moist silver oxide. It is a syrup with an alkaline reaction, and solidifies on exposure to air due to the absorption of carbon dioxide. When neutralized with haloid acids it yields the corresponding arsonium halides, and when heated with alkalis decomposes into toluene and tribenzylarsine oxide.[1417]

Chapter VI.

Heterocyclic Arsenicals.

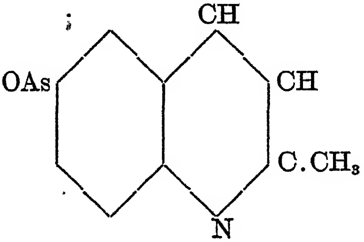
1. *Trivalent Compounds.*

Thienyl-2-dichloroarsine, 

, is obtained upon mixing arsenic trichloride and mercury dithienyl, allowing the mixture to react for 24 hours, fractionating the filtrate in an atmosphere of hydrogen at 11 mm. pressure, and rectifying the portion obtained between 116° and 130°. The product, b. p. 118-22°/11 mm., is a pale brown liquid of an unpleasant odor.[1418]

Thienyl-2-arsineoxide, $C_4H_3S.AsO$, prepared from the corresponding arsonic acid by reduction with sulfurous acid, is a white powder insoluble in water, but soluble in concentrated alkalis. It is reduced to the arseno compound by sodium hydrosulfite.[101]

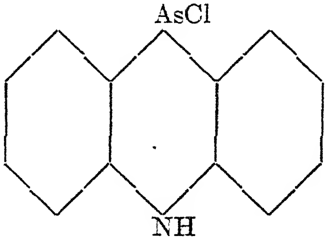
Quinaldinearsineoxide (*α-Methylquinolinearsineoxide*),



Upon reducing the corresponding arsonic acid with sodium and ethyl alcohol, and subsequently acidifying with acetic acid, the arsineoxide separates as a flocculent precipitate decomposing at 120°. It forms a picrate with picric acid in alcoholic solution.[1419]

Dithienylchloroarsine, $(C_4H_3S)_2AsCl$, is obtained either by further rectifying the fraction collected between 150° and 194°/11 mm. in the preparation of thienyldichloroarsine,[1418] or by boiling thiophene-mercurichloride (50 g.) with arsenic trichloride (35 g.) in toluene (750 c.c.) for 6-7 hours.[1420] It is a brown liquid, b. p. 219-32°/13 mm., 106-10°/0.5 mm.

Phenarsazine chloride,



, is made by heating arsenic trichloride with either diphenylamine[1421] or diphenylhydrazine.[1422] It crystallizes from carbon tetrachloride, ether, benzene or xylene in yellow needles, m. p. 192-3°, which may be sublimed in vacuo, and are soluble in concentrated sulfuric acid. When boiled with aqueous caustic soda the chlorine is replaced by a hydroxyl, while upon distillation with zinc dust, carbazole is obtained. With dry ammonia in boiling anhydrous xylene, it yields *triphenarsazineamine,*

$$\left(HN\begin{matrix} C_6H_4 \\ \\ C_6H_4 \end{matrix}As\right)_3N,$$

a difficultly soluble white precipitate, m. p. 295-300° with frothing, and soluble in glacial acetic acid with evolution of ammonia and formation of phenarsazine acetate. When heated either in vacuo at 200-300° or in high-boiling, indifferent solvents it decomposes into phenarsazine and ammonia.[1423]

On boiling phenarsazine chloride with dry pyridine, *triphenarsazine chloride,* $HN\begin{matrix} C_6H_4 \\ \\ C_6H_4 \end{matrix}As—N\begin{matrix} C_6H_4 \\ \\ C_6H_4 \end{matrix}As—N\begin{matrix} C_6H_4 \\ \\ C_6H_4 \end{matrix}AsCl$, is obtained as orange-yellow crystals, m. p. 260-3°.[1424]

Phenarsazine acetate, $HN\begin{matrix} C_6H_4 \\ \\ C_6H_4 \end{matrix}As.O.OCCH_3$, results upon boil-

ing the corresponding oxide or methyl ether with glacial acetic acid. It crystallizes in lustrous, greenish leaflets, m. p. 223-4°.[1425] The *sulfate* is an orange-yellow precipitate.

Dimethylphenarsazine chloride, $$\mathrm{HN}\begin{array}{c} \diagup\ C_6H_3(CH_3)\ \diagdown \\ \diagdown\ C_6H_3(CH_3)\ \diagup \end{array}\mathrm{AsCl}.$$ — Upon heating a mixture of equimolar quantities of di-p-tolylamine and arsenic trichloride at 180-90° and recrystallizing from glacial acetic acid or nitrobenzene, the product separates as orange-colored leaflets, m. p. 260°, soluble in concentrated sulfuric acid or the above two solvents, but difficultly so in benzene or hot alcohol.[1425]

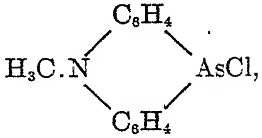
α,α-*Naphtharsazine chloride,* $$\mathrm{HN}\begin{array}{c} \diagup\ C_{10}H_6\ \diagdown \\ \diagdown\ C_{10}H_6\ \diagup \end{array}\mathrm{AsCl},$$ similarly prepared from α,α-dinaphthylamine at 210°, crystallizes from nitrobenzene in greenish-brown needles, m. p. 300°, soluble in concentrated sulfuric acid, and almost insoluble in the usual organic solvents. When distilled over copper powder it yields α,α-dinaphthylcarbazol.[1425]

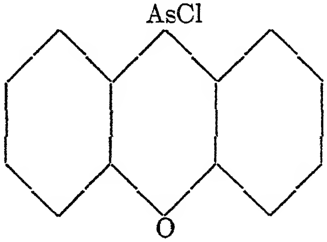
β,β-*Naphtharsazine chloride,* prepared like the α-isomer at 200°, separates from nitrobenzene in canary-yellow needles, m. p. above 300°. Its properties are similar to those of the preceding compound.[1425]

7,12-Dihydro-γ-benzophenarsazine chloride, [7-Chloro-7,12-dihydro-γ-benzophenarsazine], $$\mathrm{HN}\begin{array}{c} \diagup\ C_{10}H_6\ \diagdown \\ \diagdown\ C_{10}H_4\ \diagup \end{array}\mathrm{AsCl},$$ when recrystallized from xylene, forms canary-yellow needles, m. p. 219°, insoluble in water, soluble in xylene, glacial acetic acid, alcohol, benzene or carbon tetrachloride, is unaffected by aqueous caustic soda, and has a slight irritating action upon the mucous membranes of the nose and throat. It is prepared by gradually heating a mixture of phenyl-α-naphthylamine and arsenic trichloride up to 200°.[1426]

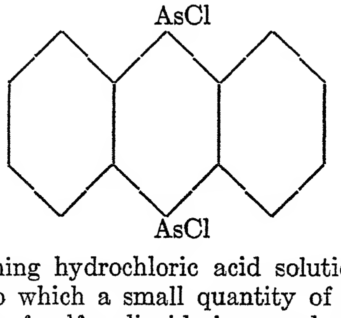
Dihydroxyphenarsazine chloride, $$\mathrm{HN}\begin{array}{c} \diagup\ C_6H_4(OH)\ \diagdown \\ \diagdown\ C_6H_4(OH)\ \diagup \end{array}\mathrm{AsCl},$$ is a

greenish-gray, crystalline powder obtained by heating 4,4′-dihydroxy-diphenylamine with arsenic trichloride.[1425]

N-Methylphenarsazine chloride,  obtained in very small yield by condensing methyldiphenylamine with arsenic trichloride, separates from a mixture of methyl alcohol and chloroform as yellowish-green needles, m. p. 203°, soluble in concentrated sulfuric acid. Concentrated nitric acid first dissolves and then nitrates it.[1427]

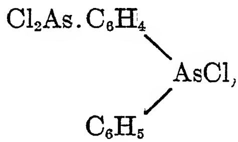
Phenoxarsine chloride,  , has been prepared by gradually heating a mixture of diphenyl ether, arsenic trichloride and a small amount of aluminium chloride up to 200°, and distilling under reduced pressure. Better yields are obtained, however, by cooling the reaction mixture, pouring off the mother liquor from the crystals formed, and reheating the solution. The product, which may be recrystallized from alcohol, ether or glacial acetic acid, is readily soluble in benzene, acetone or chloroform, moderately so in alcohol, ether or glacial acetic acid, and slightly in ether or light petroleum. It is stable toward boiling water or aqueous caustic soda, and has an irritating effect upon the mucous membrane.[1428]

Diphenylenediarsine dichloride (*Arsanthrenechloride*),

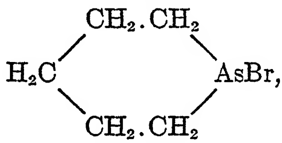


Through a warm fuming hydrochloric acid solution of diphenylarsinic acid-o-arsonic acid, to which a small quantity of potassium iodide has been added, a current of sulfur dioxide is passed, and the resulting oily product dried and distilled. The fraction coming over between 200°

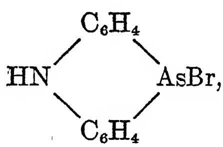
and 290° consists of a mixture of the above compound and diphenylchloroarsine-2-dichloroarsine, which are separated either by fractional crystallization from benzene or chloroform, or by triturating in a mortar with ether in which arsanthrenechloride is difficultly soluble. The compound crystallizes from carbon tetrachloride in spear-shaped crystals, m. p. 182-3°, readily soluble in benzene, chloroform, carbon bisulfide or ligroin, and difficultly in ether. It is easily hydrolyzed by water.[1429]

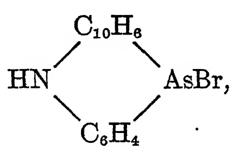
Diphenylchloroarsine-2-dichloroarsine,  crystallizes in white needles, m. p. 153-5°, easily soluble in benzene, chloroform, carbon tetrachloride or hot ligroin, and moderately in ether. Its solubilities are generally greater than those of arsanthrene chloride.[1430]

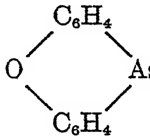
Pentamethylenebromoarsine (*Arsepidine bromide*),

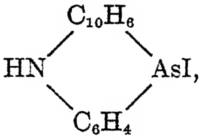


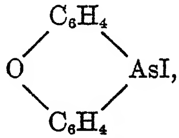
is an impure, reddish oil obtained when dibromomethylarsepidine is warmed or allowed to stand in vacuo.[1431]

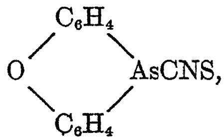
Phenarsazine bromide,  forms yellow crystals upon heating diphenylamine with arsenic tribromide.[1425]

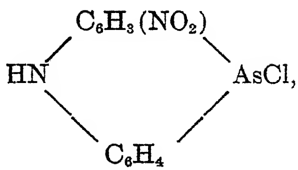
7,12-Dihydro-γ-benzophenarsazine bromide, [*7-Bromo-7,12-dihydro-γ-benzophenarsazine*],  results upon refluxing the corresponding phenoxy compound with an excess of concentrated hydrobromic acid. It crystallizes from xylene in dark yellow needles, m. p. 227°, soluble in benzene, toluene, xylene or glacial acetic acid, insoluble in water, and unaffected by dilute alkalis.[1422]

Phenoxarsine bromide, , is obtained from the corresponding chloride by treating with sodium bromide in warm methyl alcoholic solution, or by refluxing the corresponding oxide with concentrated hydrobromic acid. It consists of yellow crystals, m. p. 128°.[1432]

7,12-Dihydro-γ-benzophenarsazine iodide, [*7-Iodo-7,12-dihydro-γ-benzophenarsazine*], , derived from the corresponding phenoxy compound or oxide by warming with dilute hydriodic acid, crystallizes from xylene in beautiful red needles, m. p. 205°, soluble in benzene, toluene, xylene or glacial acetic acid.[1422]

Phenoxarsine iodide, , crystallizes from ethyl alcohol in bright yellow needles, m. p. 144°, easily soluble in benzene, slightly so in methyl or ethyl alcohol. It is prepared from the corresponding chloride by treating with potassium iodide in methyl alcoholic solution.[1432]

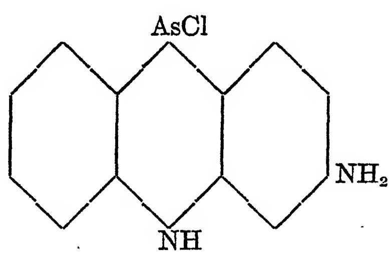
Phenoxarsine thiocyanate, , prepared from the chloride and potassium thiocyanate in ethyl alcoholic solution, crystallizes in bright yellow, monoclinic prisms, m. p. 129°.[1433]

o- and p-Nitrophenarsazine chlorides, , to-

gether with the corresponding dinitro compound are obtained upon nitrating phenarsazine chloride. The two isomeric mononitro derivatives are dissolved upon digesting the mixture with cold acetone, the solution concentrated and allowed to cool, whereupon the last trace of dinitro compound separates out. The filtrate is then evaporated to dryness, the residue extracted with warm benzene, and the resulting solution evaporated to dryness. The ortho derivative is then removed by means of ether. It crystallizes from benzene or glacial acetic acid in scarlet needles, m. p. 156°. The para isomer separates from glacial acetic acid as dark greenish-yellow leaflets yielding a carmine-red solution with hydrogen peroxide in dilute alkaline solution, while with the ortho compound a brownish-red salt is obtained.[1434]

p,p′-Dinitrophenarsazine chloride, $HN\left<\begin{array}{c}C_6H_3(NO_2)\\ \\ C_6H_3(NO_2)\end{array}\right>AsCl$, is obtained upon nitrating phenarsazine chloride with fuming nitric acid in glacial acetic acid solution at 18-20°. On standing, the dinitro compound separates out along with the o- and p-mononitro derivatives which are removed by cold acetone. The dinitro product crystallizes from nitrobenzene in light yellow needles, m. p. above 300°, which are oxidized to the corresponding arsazinic acid upon warming the dilute alkaline suspension with perhydrol. By adding a few drops of aqueous caustic soda to its alcoholic suspension, a reddish-violet solution of a quinoid-aci-nitro salt is obtained, which is decomposed upon the addition of water.[1435]

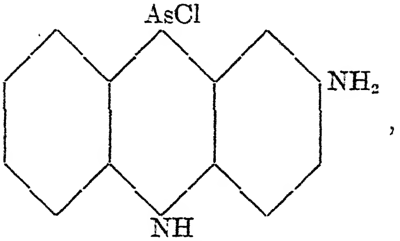
m-Aminophenarsazine chloride,



,

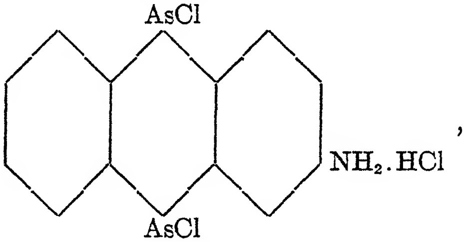
is isolated in the form of yellowish-green leaflets of its hydrochloride upon heating 3-aminodiphenylamine and arsenic trichloride at 140-70° for five hours. When treated with sodium carbonate it forms the corresponding arsineoxide, while upon oxidation with perhydrol in alkaline solution it yields the arsazinic acid.[1436]

p-Aminophenarsazine chloride,



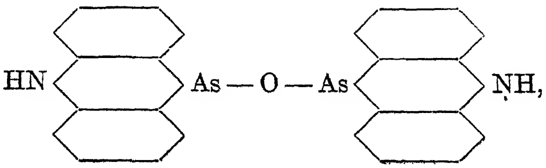
is the main product formed in the reduction of the corresponding nitro arsazinic acid with powdered iron and a small amount of ferric chloride, but it is more easily obtained by reducing the corresponding amino arsazinic acid with sulfur dioxide in concentrated hydrochloric acid containing a little hydriodic acid. It is known only in the form of its hydrochloride, which consists of lustrous, yellowish-green leaflets soluble in water, and extremely irritating to the mucous membranes of the eyes, nose and throat. It yields the corresponding oxide with soda, and forms a violet-red dyestuff with hydrogen peroxide in alkaline suspension.[1437]

Hydrochloride of m-aminoarsanthrene chloride,



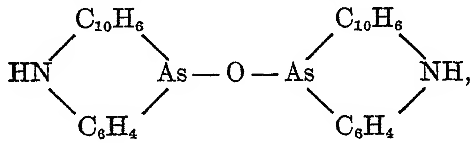
results when a solution of m-aminodiphenylarsinic-o-arsonic acid in concentrated hydrochloric acid, to which a trace of potassium iodide has been added, is reduced with sulfur dioxide at 60-70°. It separates in colorless, amorphous flakes which may be occasionally obtained crystalline by saturating its dilute aqueous solution with hydrogen chloride. It yields no dyestuffs with oxidizing agents in alkaline medium, but when treated with sodium carbonate in aqueous solution it is converted into the oxide which upon warming with perhydrol is oxidized to m-aminoarsanthrenic acid.[1438]

Phenarsazine oxide,

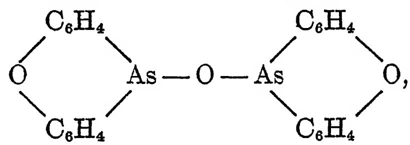


may be derived from phenarsazine chloride by treatment with alkalis,[1439] crystallizing from 80 per cent acetic acid, in pale yellow crystals, and from nitrobenzene or pyridine in colorless leaflets, m. p. above 350°. It is extremely irritating to the mucous membrane of the nose and mouth, is practically insoluble in alcohol, acetone, benzene, chloroform, ether, alkalis or dilute acids, readily soluble in acetic or concentrated sulfuric acid, is unaffected by alkalis even on heating, and behaves like an acid anhydride with alcohols forming ethers. Upon boiling with glacial acetic acid it is converted into the corresponding acetate.

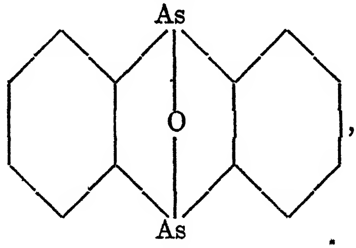
7,12-Dihydro-γ-benzophenarsazine oxide,



is a pale yellow precipitate which does not darken or melt below 250°, is soluble in glacial acetic acid, and insoluble in benzene, xylene or carbon tetrachloride. It is formed upon adding ammoniacal silver oxide to a xylene solution of the corresponding chloride.[1440]

Phenoxarsine oxide,  results upon treating phenoxarsine chloride with either alkalis, sodium methylate or ethylate, or with ammonia in alcoholic or benzene solution. It crystallizes from alcohol in needle-like fibers, from hot benzene in large diamond-shaped crystals, m. p. 182°, soluble in all common organic solvents, but insoluble in aqueous alkalis. It is readily converted into the corresponding halide by haloid acids.[1432]

Diphenylenediarsineoxide (Arsanthrene oxide),



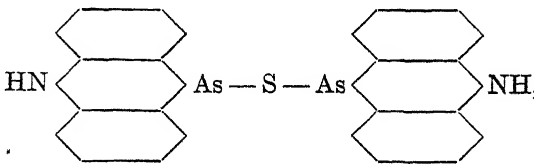
prepared by treating the corresponding dichloride with aqueous sodium carbonate, crystallizes from alcohol in tetragonal leaflets, m. p. 196°,

sublimes undecomposed at low pressures in an atmosphere of carbon dioxide, is easily soluble in benzene, chloroform or carbon bisulfide, and difficultly in ether or alcohol. The ethereal solution becomes turbid on standing, due to the formation of a very difficultly soluble unidentified substance. The oxide is converted into the dichloride by treatment with ethereal hydrochloric acid in the presence of calcium chloride. Upon reduction it yields arsanthrene.[1441]

Methoxyphenarsazine, $HN{<}{C_6H_4 \atop C_6H_4}{>}As.O.CH_3$, from the chloride and sodium methylate, crystallizes in long, colorless needles, m. p. 194°, easily saponified by boiling water or alkalis to the corresponding oxide.[1442]

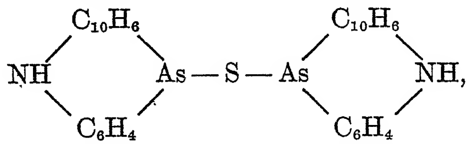
7-Methoxy-7,12-dihydro-γ-benzophenarsazine, $HN{<}{C_{10}H_6 \atop C_6H_4}{>}AsOCH_3$, similarly prepared, separates from xylene in almost colorless crystals, m. p. 209°, soluble in benzene, acetone or carbon tetrachloride, insoluble in water, and decomposed by aqueous caustic soda. The *ethoxy* compound consists of colorless crystals, m. p. 165°, soluble in the common organic solvents, and decomposed by caustic soda. The *n-propoxy* derivative forms pale yellow crystals, m. p. 152°, soluble in benzene, acetone or carbon tetrachloride and attacked by hot alkalis. The *n-butoxy* compound partially softens at 120°, but does not melt completely up to 260°, is soluble in benzene, acetone or glacial acetic acid, and is unstable in alkalis. The *phenoxy* compound crystallizing in yellow needles, m. p. 179°, and the almost colorless *benzyl* ether, m. p. 154°, behave like the alkyl ethers with various solvents or caustic alkalis.[1443]

Phenarsazine sulfide,

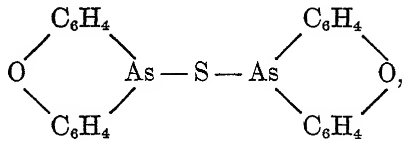


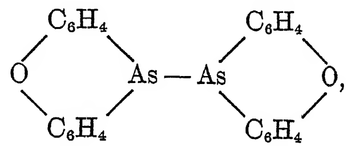
is obtained upon saturating a methyl alcoholic solution of the corresponding oxide or methoxy compound with hydrogen sulfide. It crystallizes from chloroform or benzene-acetone in felted needles or leaflets, m. p. 262°, from which hydrogen sulfide is split off on heating in high-boiling solvents, yielding phenarsazine.[1424]

7,12-Dihydro-γ-benzophenarsazine sulfide,



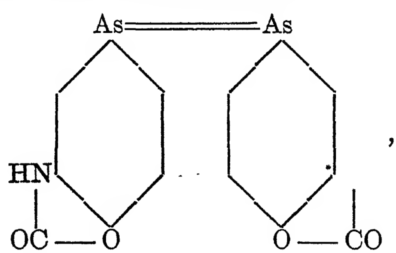
from the corresponding chloride and hydrogen sulfide in absolute ethyl alcohol, is a yellow precipitate, m. p. 204-5°, insoluble in the common organic solvents.[1422]

6-Phenoxarsine sulfide,  prepared like the preceding compound, crystallizes from glacial acetic acid in straw-colored needles, m. p. 161°, and insoluble in the usual solvents.[1433]

6,6-Bisphenoxarsine (Phenoxycacodyl),  results upon reducing the corresponding oxide with phosphorous acid in boiling absolute alcoholic solution. It crystallizes in bright yellow needles, m. p. 159°, soluble in benzene, chloroform or hot acetic acid, slightly in light petroleum-ether, and insoluble in hot or cold water, alcohol, ether, hot dilute alkalis or hydrochloric acid. Upon exposure to air it slowly oxidizes to a mixture of the oxide and phenoxarsinic acid.[1433]

Arsenothiophene, $S.C_4H_3As = As.C_4H_3.S$, is obtained by the reduction of the corresponding arsineoxide with sodium hydrosulfite.[101]

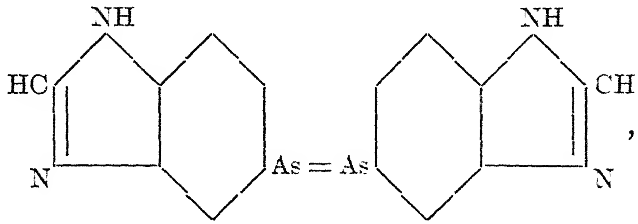
3,4,3′,4′-Tetrahydroarsenobenzodioxazolone,



is derived from the corresponding arsonic acid by reducing its alkaline solution with sodium hydrosulfite in the presence of magnesium chloride, at 60° in an atmosphere of carbon dioxide. It forms a pale yellow,

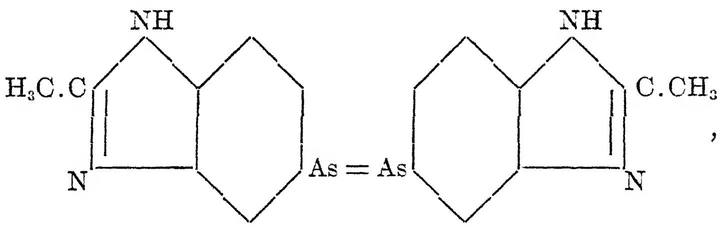
granular powder, insoluble in water, aqueous sodium carbonate or the usual organic solvents, but readily soluble in aqueous sodium hydroxide. Its sodium salt is a pale yellow, fairly stable powder readily soluble in water, sparingly in alcohol, and insoluble in ether.[1441]

5,5′-Arseno-1,3,1′,3′-benzodiazole,



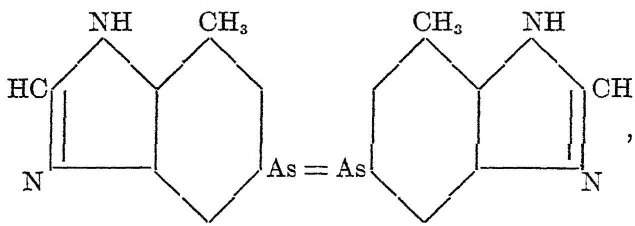
similarly prepared from the corresponding arsonic acid, is a bright yellow powder practically insoluble in water, methyl alcoholic hydrochloric acid or the usual organic solvents, but dissolves in dilute hydrochloric or 50 per cent acetic acid. The dihydrochloride contains $2H_2O$, and is a pale yellow powder soluble in water, very sparingly in methyl or ethyl alcohol, and insoluble in acetone or ether.[1111]

2,2′-Dimethyl-5,5′-arseno-1,3,1′,3′-benzodiazole,



prepared like the two preceding compounds, yields a pale yellow dihydrochloride containing $3H_2O$, soluble in water, practically insoluble in ether, acetone, methyl or ethyl alcohol.[1109]

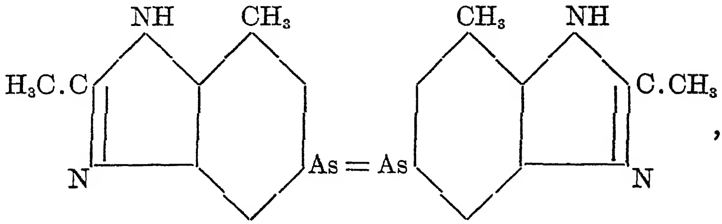
7,7′-Dimethyl-5,5′-arseno-1,3,1′,3′-benzodiazole,



is a pale yellow powder, insoluble in water or the usual organic solvents, but moderately soluble in acetic acid. The dihydrochloride is a

pale yellow, granular powder soluble in water but insoluble in organic solvents.[1445]

2,7,2′,7′-Tetramethyl-5,5′-arseno-1,3,1′,3′-benzodiazole,



and its dihydrochloride, resemble the preceding arseno compounds with regard to method of preparation, physical and chemical properties.[1445]

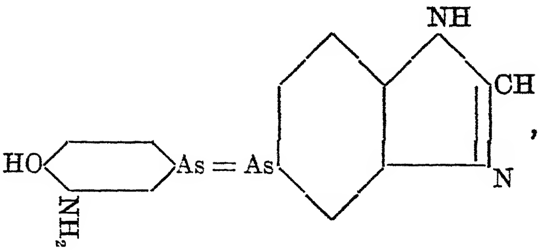
4′-Arsenodi(1-phenyl-2,3-dimethyl-4-amino-5-pyrazolone) is obtained by reducing the corresponding nitroso arsonic acid with sodium hydrosulfite at 60-65°. Its dihydrochloride, prepared by dissolving the base in methyl alcoholic hydrochloric acid and precipitating with ether, forms yellow crystals easily soluble in water or methyl alcohol.[1446]

N-4′-Arsenodi(1-phenyl-2,3-dimethyl-4-amino-5-pyrazolone)-monoacetic acid, prepared by heating an aqueous suspension of the above base with bromoacetic acid at 60°, is a yellowish powder soluble in hydrochloric acid, aqueous sodium hydroxide or carbonate, difficultly so in water, and insoluble in alcohol. By employing an excess of bromoacetic acid in the above reaction, a *diacetic derivative* is obtained.[1446]

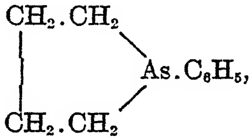
N-4′-Arsenodi(1-phenyl-2,3-dimethyl-4-amino-5-pyrazolone)-monomethylenesulfoxylic acid is obtained by the action of formaldehyde sulfoxylate on either the hydrochloride of 4′-arsenodi (1-phenyl-2,3-dimethyl-4-amino-5-pyrazolone) or 1-(phenyl-4′-arsonic acid)-2,3-dimethyl-4-nitroso-5-pyrazolone. It forms a yellowish powder soluble in aqueous alkalis or hydrochloric acid, difficultly in water, and insoluble in alcohol. Its yellow alkali salts are easily soluble compounds. A *dimethylenesulfoxylic acid derivative* is obtained with a larger excess of formaldehyde sulfoxylate.[1446]

N-4′-Arsenodi(1-phenyl-2,3-dimethyl-4-amino-5-pyrazolone)methylenesulfurous acid, is similarly prepared by employing sodium bisulfite and formaldehyde. It is a yellow powder soluble in acids or alkalis, and insoluble in water, ether or benzene.[1446]

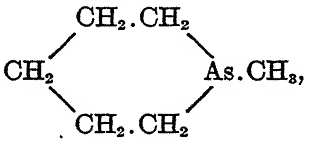
5-(3-Amino-4-hydroxyphenylarseno)benzimidazole [3′-Amino-4′-hydroxy-1,3-diazole-5-1′-arsenobenzene],



results upon reducing a mixture of molecular proportions of 3-amino-4-hydroxyphenylarsonic and 1,3-benzodiazole-5-arsonic acids with sodium hydrosulfite in the usual manner. It is readily soluble in aqueous sodium hydroxide or methyl alcoholic hydrochloric acid. The hydrochloride is a pale yellow powder containing $3H_2O$, readily soluble in water or methyl alcohol, less so in ethyl alcohol, and almost insoluble in ether or acetone. It decomposes at 206° without previous melting.[1447]

Phenylcyclotetramethylenearsine,  obtained in absolute ethereal medium by the interaction of phenyldichloroarsine and the Grignard reagent prepared from 1,4-dibromobutane, is a colorless, mobile oil with a faint, unpleasant odor, b. p. 128.5°/15-16 mm., D^{17}_{4} 1.2824, D^{20}_{4} 1.2794, unaffected by air or light at ordinary temperature, easily soluble in alcohol, ether or most organic solvents, and but slightly in water. Its mercurichloride crystallizes from hot chloroform in beautiful hexagonal leaflets, m. p. 160-2°, easily soluble in pyridine but difficultly in the other organic solvents.[1448]

Methylcyclopentamethylenearsine (*Methylarsepidine*),



prepared from methyldichloroarsine and the Grignard reagent from 1,5-dichloropentane in the absence of air, is a colorless, refractive liquid with an odor of mustard oil, D 1.218/18°, b. p. 156°/760 mm., 76°/36 mm., 65°/20-22 mm., soluble in alcohol, ether, ligroin, benzene or carbon tetrachloride, insoluble in water or hydrochloric acid, and oxidizing in air to a colorless oxide. It slightly reduces ammoniacal silver nitrate

or alkaline permanganate solution; combines additively with halogens, methyl iodide or chloroplatinic acid, and yields free arsenic with strong reducing agents. It is decomposed when heated in a closed tube either alone or with calcium oxide; with hydriodic acid and red phosphorus at 230° for five hours it yields arsine, arsenic triiodide and a very volatile, inflammable liquid, probably pentane. It undergoes complete oxidation when heated with concentrated nitric acid in a sealed tube at 250-80° for eight hours.[1449]

The platinichloride, $\left[(CH_2)_5{>}As \begin{array}{l} \diagup CH_3 \\ - H \\ \diagdown Cl \end{array} \right]_2 PtCl_4$, is a pale yellow powder, m. p. 163°, soluble in alcohol but sparingly in water.[1450]

Ethylcyclopentamethylenearsine (*Ethylarsepidine*), $(CH_2)_5As.C_2H_5$, similarly prepared from ethyldichloroarsine and a Grignard solution of 1,5-dibromopentane, is a liquid with an ethereal odor, b. p. 62-4°/12.5 mm.[1297]

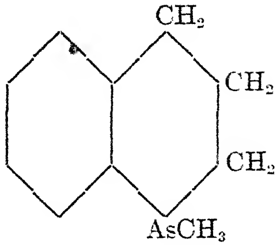
Phenylcyclopentamethylenearsine (*Phenylarsepidine*),

$$(CH_2)_5As.C_6H_5,$$

is a colorless, viscous oil of a faint, unpleasant odor, b. p. 153-4°/18-20 mm. in carbon dioxide, miscible with ether, benzene or carbon tetrachloride, easily soluble in hot alcohol, but only slightly so in water. It may be obtained either like the corresponding methyl and ethyl derivatives, or by condensing 1,5-dichloro- or dibromo pentane with phenyldichloroarsine by means of metallic sodium in absolute ether in the presence of a small quantity of ethyl acetate.[1451]

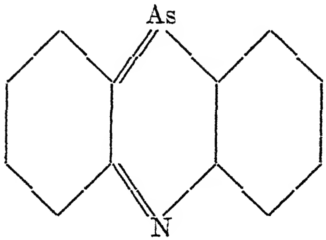
Its readily decomposable mercuriacetate crystallizes in long needles easily soluble in the usual solvents. With calcium chloride in methyl alcoholic solution it yields the corresponding mercurichloride which crystallizes from chloroform in long needles, m. p. 201.5-2°.[1452]

4-Methylphenylarsepidine, $(CH_2)_5As.(C_6H_4.CH_3)$, prepared like the corresponding phenyl compound, is a colorless, viscous oil having a faint, unpleasant odor, b. p. 162-3°/20 mm., 177-8°/50 mm. in carbon dioxide, readily soluble in ether, ligroin, benzene, carbon tetrachloride or hot alcohol, and slightly so in water. Its mercurichloride crystallizes from chloroform in long needles, m. p. 175°, very difficultly soluble in all solvents except pyridine, in which it readily dissolves.[1453]

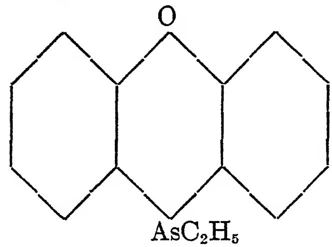
As-Methyltetrahydroarsinoline,  .—A mixture of γ-phenylpropylmethylchloro- or bromoarsine, carbon bisulfide and aluminium chloride is gently boiled for three hours, decomposed by ice, and the whole acidified and extracted with carbon tetrachloride. Upon distilling the extract under diminished pressure, a slightly impure product is obtained as a colorless, highly refractive liquid, b. p. 140°/14 mm. with an odor slightly resembling that of quinoline. It slowly oxidizes in air, and is soluble in concentrated sulfuric acid. Another method of preparation consists in gently heating the above chloroarsine with benzene in the presence of aluminium chloride.

The platinichloride is a yellow, microcrystalline powder, m. p. 170°, the picrate and picronolate are well-defined, yellow crystalline salts, while with methyl iodide the arsinoline forms an additive compound which crystallizes from alcohol or water in colorless prisms, m. p. 235°.[219]

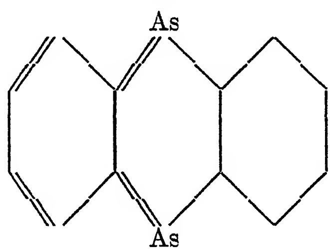
Trithienylarsine, $(S.C_4H_3)_3As$, formed along with the mono and dithienylhalogenated arsines by the interaction of mercury dithienyl and arsenic trichloride, is obtained from the fraction boiling above 190°/11 mm. by concentrating and redistilling with the aid of a Gaede pump. It is a pale yellowish-green, viscous, almost odorless liquid, b. p. 199-200.5°/0.5 mm.[1418]

Phenarsazine,  , is prepared by boiling phenarsazine methyl ether with freshly distilled diphenylmethylamine. An impure product may be obtained by heating any of the phenarsazine derivatives in vacuo or high-boiling solvents above 200°, when the residue attached to the arsenic and the hydrogen of the imino group are split off. The dry, coarsely crystalline product melts at 310°, is stable in dry air, easily soluble in nitrobenzene, diphenylmethylamine, ether or concentrated sulfuric acid, and difficultly in hot xylene. Moisture converts it into the corresponding oxide. It forms addition products with

alcohols, phenol, glacial acetic acid, amines or hydrochloric acid, all of which, with the exception of the last, may be resolved into their original components.[1454]

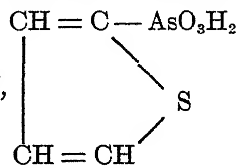
As-Ethylphenoxarsine, , is derived from the corresponding chloro derivative by treating with ethylmagnesium iodide in absolute ether. It crystallizes in white needles, m. p. 218°, soluble in alcohol, ether or benzene, and forms an arsonium compound with ethyl iodide.[1455]

Diphenylenediarsine (Arsanthrene),



Prepared by reducing the corresponding dichloride with zinc and fuming hydrochloric acid in warm alcohol, or by boiling the oxide with alcoholic phenylhydrazine. It crystallizes in orange-yellow, rhombic leaflets, m. p. 340°, very difficultly soluble in glacial acetic acid, pyridine or phenylhydrazine, and insoluble in the usual solvents.[1441]

2. *Pentavalent Compounds.*

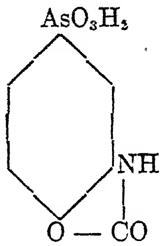
Thienyl-2-arsonic acid, 

Thiophene-2-mercurichloride is treated with arsenic trichloride, the filtered solution rendered alkaline, and oxidized with hydrogen peroxide, when a mixture of the arsonic and corresponding arsinic acids is obtained. These are converted into the sodium salts in the presence of

absolute alcohol, the arsonate crystallizing out, while the arsinate remains in solution. The free arsonic acid crystallizes from water in needles, m. p. 135.5°, easily soluble in water, alcohol, ethyl acetate or acetone, but difficultly in ether, chloroform or ligroin. At 105-8° it is converted into the anhydride, $S.C_4H_3.AsO_2$. On reduction with sulfurous acid, it forms the corresponding arsineoxide.

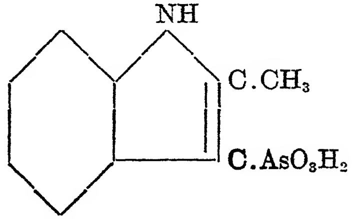
Salts.—The monosodium salt consists of rhombic scales easily soluble in water; the neutral magnesium salt is a white, crystalline precipitate; the acid barium salt, which is a white, crystalline precipitate soluble in cold but less so in hot water, is converted into the neutral salt on boiling with ammonia; the disilver salt is an amorphous, white precipitate soluble in ammonia or acids.[101]

3,4-Dihydrobenzoxazolone-1-arsonic acid,



.—An alkaline solution of 3-amino-4-hydroxyphenylarsonic acid is treated with a toluene solution of carbonyl chloride at low temperature, and the aqueous layer first extracted with ether, and then acidified with hydrochloric acid, where the oxazolone separates as a sandy, crystalline precipitate. It crystallizes from boiling water in colorless, prismatic needles decomposing at 250° without melting, sparingly soluble in alcohol, and readily in boiling water. On reduction with sodium hydrosulfite it yields the corresponding arseno compound.[1444]

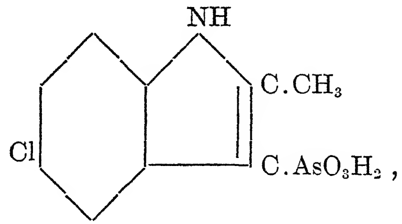
2-Methylindole-3-arsonic acid (Methylketolearsonic acid),



, results upon warming a mixture of methyl ketole and arsenic acid. It crystallizes in white needles, m. p. 180-2°, easily soluble in alcohol, glacial acetic acid or dilute caustic soda, but insoluble in the other organic solvents. Its sodium salt, containing $2\frac{1}{2}H_2O$, melts at 225-35° with decomposition, and is readily soluble in water, while the quinine salt separates from diluted methyl or ethyl alcohol in fine needles

sintering at 155°, melting at 170-2°, and insoluble in chloroform or ether.[1456]

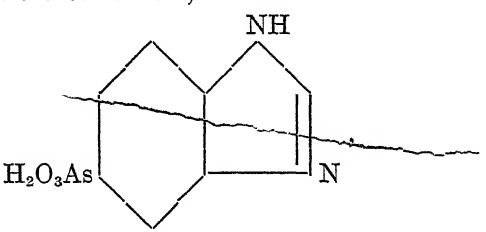
5-Chloro-2-methylindole-3-arsonic acid,



is obtained by treating a toluene solution of 5-chloro-2-methylindole with a solution of arsenic acid in alcohol, and refluxing the mixture for 2 hours. The compound crystallizes from dilute alcohol, and melts at 185-6° with decomposition.[1456]

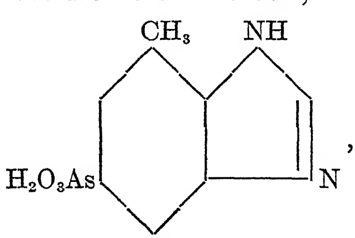
α-Naphthindolearsonic acid, $C_{12}H_8N.AsO_3H_2$, similarly prepared from α-naphthindole, is difficultly soluble in alcohol and insoluble in the other organic solvents.[1456]

1,3-Benzodiazole-5-arsonic acid,



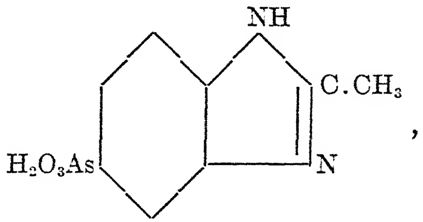
is derived from 3,4-diaminophenylarsonic acid by refluxing with glacial formic acid. It crystallizes from water in clusters of minute prisms decomposing at about 297°.[1457]

7-Methyl-1,3-benzodiazole-5-arsonic acid,



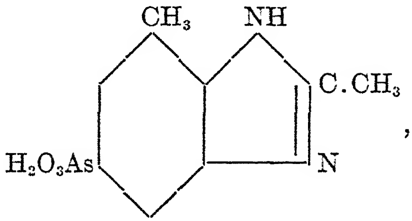
similarly prepared from 3,4-diamino-5-methylphenylarsonic acid, crystallizes in minute, prismatic needles, m. p. 300° with decomposition, sparingly soluble in water.[1458]

2-Methyl-1,3-benzodiazole-5-arsonic acid,



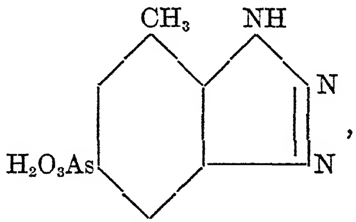
is formed upon heating 3,4-diacetyldiaminophenylarsonic acid with ten parts of water in a sealed tube at 130°. It crystallizes in minute needles with $2\frac{1}{2}H_2O$ and decomposes at 270°.[1169]

2,7-Dimethyl-1,3-benzodiazole-5-arsonic acid,



crystallizes from hot water in minute, prismatic needles containing $2H_2O$. It is obtained by the prolonged action of boiling acetic acid upon 3,4-diamino-5-methylphenylarsonic acid.[1445]

7-Methyl-1,2,3-benzotriazole-5-arsonic acid,



is formed upon treating a dilute hydrochloric acid solution of 3,4-diamino-5-methylphenylarsonic acid with one molecular proportion of sodium nitrite. It crystallizes from 50 per cent alcohol in lustrous needles, decomposing above 280°, sparingly soluble in water, but more readily in alcohol.[1458]

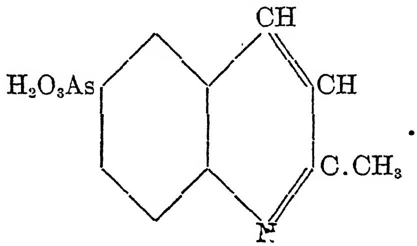
1-(Phenyl-4′-arsonic acid)-3-methyl-5-chloropyrazole.—1,4′-Aminophenyl-3-methyl-5-chloropyrazole is diazotized with sodium nitrite in hydrochloric acid solution, treated with an alkali arsenite, and the product precipitated by acidifying. When rapidly heated it melts at 192-5°,

forming the corresponding anhydride, which upon continued heating resolidifies and decomposes above 290°.[1446]

1-(Phenyl-4′-arsonic acid)-3-methyl-5-pyrazolone results upon diazotizing p-arsanilic acid, reducing the diazo solution with stannous chloride, and condensing the resulting phenylhydrazinearsonic acid with acetoacetic ester. The compound is easily soluble in alkalis, but only sparingly in cold water.[1446]

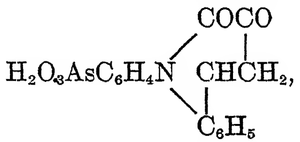
1-(Phenyl-4′-arsonic acid)-2,3-dimethyl-5-pyrazolone is prepared by methylating either of the two preceding compounds with dimethyl sulfate at 120°, and subsequently heating with aqueous sodium carbonate at 95°. It is easily soluble in dilute acids or alkalis.[1446]

Quinaldinearsonic acid (α-Methylquinolinearsonic acid),



p-Arsanilic acid is treated with acetaldehyde, and the resulting product dissolved in hydrobromic acid (d, 1.49). The yellow, crystalline substance which separates is then washed with water, dissolved in alcohol, and reprecipitated with water. The product begins to decompose at 140°, is completely charred at 170°, is soluble in alcohol, and insoluble in water, ether, alkalis or mineral acids. Upon reduction with sodium and ethyl alcohol it yields the corresponding arsineoxides.[1459]

*1-(4′-Arsonophenyl)-2-phenyl-4,5-diketopyrrolidine,**



results upon refluxing a mixture of equimolar amounts of p-arsanilic acid and benzaldehyde in absolute alcohol until most of the acid is dissolved, adding one molecular proportion of pyruvic acid or ethyl pyruvate, and boiling for 3½-4 hours. The crude product, which separates from the filtrate upon cooling, may be purified by recrystallizing

NOTE. This compound had previously been described as 2-Phenylquinoline-4-carboxylic acid-6-arsonic acid.

from alcohol, and consists of a cream-colored powder, m. p. 186-7° with decomposition. It forms a neutral disodium salt, a slightly alkaline trisodium salt, and gives off one mole of carbon dioxide upon boiling in ethyl benzoate. From a solution of the disodium salt, copper sulfate precipitates a green salt; silver, lead, mercurous, mercuric and cadmium nitrates yield light yellow salts, while with cobalt and ferric nitrates, reddish-brown salts are formed.[1460, 151]

1 - (4′ - Arsonophenyl) - 2 - (4′ - chlorophenyl) -4,5-diketopyrrolidine is similarly obtained, employing 4-chlorobenzaldehyde. It is a white powder, m. p. 163-5° with decomposition.[151]

1-(4′-Arsonophenyl) - 2 - (2′ - methoxyphenyl) - 4,5 - diketopyrrolidine, from salicylaldehyde methyl ether, is a pale yellow powder, m. p. 173-6° with decomposition.[151]

1-(4′-Arsonophenyl) - 2 - (4′ - methoxyphenyl) - 4,5 - diketopyrrolidine, similarly prepared from anisaldehyde, consists of almost white crystals, m. p. 164-5° with decomposition.[151]

1-(4′-Arsonophenyl)-2-(3′,4′-methylene dioxyphenyl)-4,5-diketopyrrolidine, from p-arsanilic acid, piperonal and pyruvic acid, is a light yellow powder, m. p. 176-8° with decomposition.[151]

1-(4′-Arsono-3′-methylphenyl)-2-phenyl-4,5-diketopyrrolidine from 4-amino-2-methylphenylarsonic acid, benzaldehyde and pyruvic acid, is a cream-colored powder, m. p. 180-6° with decomposition.[151]

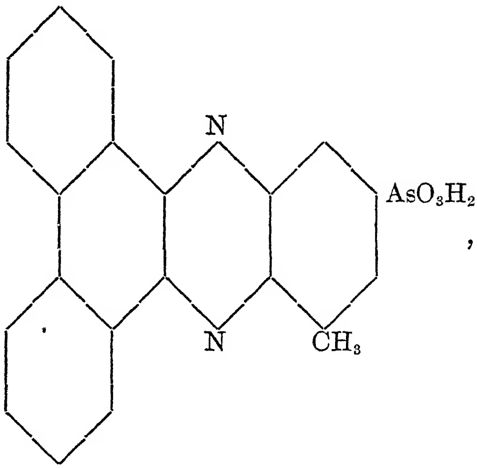
1-(4′-Arsono-3′-methoxyphenyl)-2-phenyl-4,5-diketopyrrolidine, similarly obtained by employing 4-amino-2-methoxyphenylarsonic acid, is a yellow powder melting at 175-6° with decomposition.[151]

Phenanthrophenazinearsonic acid (*Diphenylenequinoxalinearsonic acid*),

$$H_2O_3AsC_6H_4\begin{array}{l} \diagup N = C.C_6H_4 \\ \phantom{\diagup N = {}} | \quad\;\; | \\ \diagdown N = C.C_6H_4 \end{array}$$

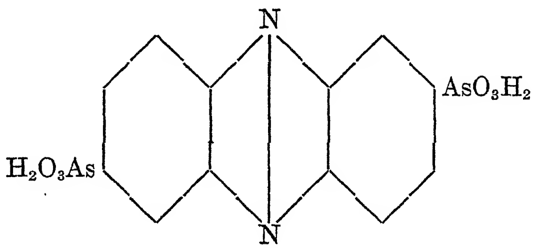
, is derived from 3,4-diaminophenylarsonic acid by treating its hot methyl alcoholic solution with a hot glacial acetic acid solution of phenanthrenequinone (1 mol.). The pale yellow product neither melts nor decomposes below 300°, is very sparingly soluble in the usual solvents, but dissolves in aqueous sodium carbonate, concentrated sulfuric or nitric acid.[1106]

4-Methylphenanthrophenazine-2-arsonic acid,



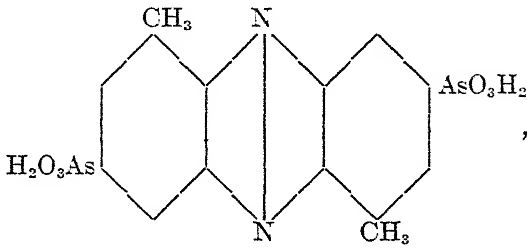
is obtained by condensing molecular proportions of 3,4-diamino-5-methylphenylarsonic acid and phenanthroquinone in acetic acid solution. It forms an amorphous, yellow powder sparingly soluble in water or the usual organic solvents, but readily in concentrated mineral acids. It also dissolves in dilute sodium hydroxide or carbonate, the sodium salt being precipitated upon the addition of an excess of the reagent.[1458]

Phenazine-2,7-bisarsonic acid,



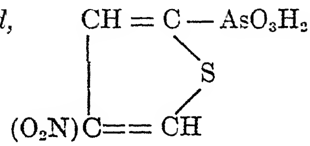
prepared by treating a warm dilute sulfuric acid solution of p-arsanilic acid with ammonium persulfate, and purifying through the sodium salt, crystallizes with $1H_2O$, does not melt below 300°, is insoluble in water or the usual organic solvents, very sparingly in alcohol or acetic acid, and dissolves in concentrated sulfuric acid with a blood-red coloration. At 150° it loses $2H_2O$, forming an inner anhydride. Its tetrasodium salt consists of a buff-colored crystalline powder containing $11H_2O$, soluble in cold water but insoluble in alcohol. On standing in vacuo it loses $1\frac{1}{2}H_2O$ and turns bright red in color.[1461]

4,9-Dimethylphenazine-2,7-bisarsonic acid,



similarly prepared from 4-amino-3-methylphenylarsonic acid, is a buff-colored powder having the same properties as the preceding compound.[1462]

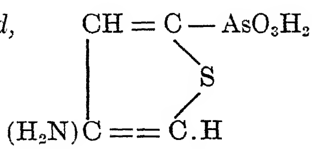
5-Nitrothienyl-2-arsonic acid,



obtained by nitrating the corresponding arsonic acid with a mixture of fuming nitric and concentrated sulfuric acids, crystallizes from water in small prisms, melting at 194° when rapidly heated, but remaining unmelted up to 250° on slow heating. It is soluble in alkalis, boiling glacial acetic acid, alcohol or water, sparingly in cold water and insoluble in chloroform or ether.[102]

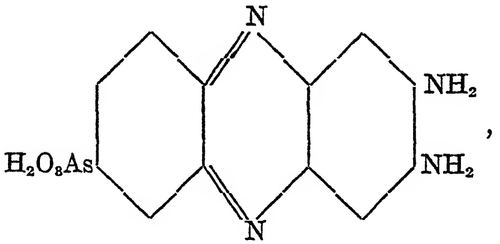
4-Nitroso-1-(phenyl-4′-arsonic acid)-2,3-dimethyl-5-pyrazolone is a very unstable, bluish-green substance obtained by treating 1-(phenyl-4′-arsonic acid)-2,3-dimethyl-5-pyrazolone with sodium nitrite and dilute sulfuric acid. Upon reduction with sodium hydrosulfite at 60-5°, it yields the corresponding arseno compound.[1446]

5-Aminothienyl-2-arsonic acid,



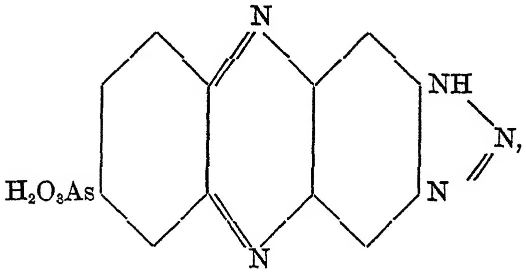
results upon reducing the corresponding nitro acid either with sodium hydrosulfite, or with sodium amalgam in methyl alcoholic solution. It crystallizes in leaflets, m. p. 194° with complete decomposition, soluble in boiling glacial acetic acid, but difficultly in the other organic solvents. Its hydrochloride is a crystalline mass soluble in water or alcohol, but insoluble in ether.[102]

2,3-Diaminophenazine-7-arsonic acid,



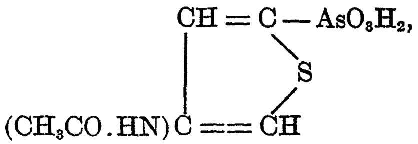
is obtained as a brick-red acetate by condensing 3-nitro-4-triazophenylarsonic acid with o-phenylenediamine in glacial acetic acid medium, and precipitating with ether. It is readily soluble in glacial acetic acid or dilute hydrochloric acid, sparingly in alcohol, and insoluble in alkalis. By neutralizing the acid solution with ammonia, the impure base is precipitated. The latter cannot be readily purified.[1463]

Azimidophenazine-7-arsonic acid,



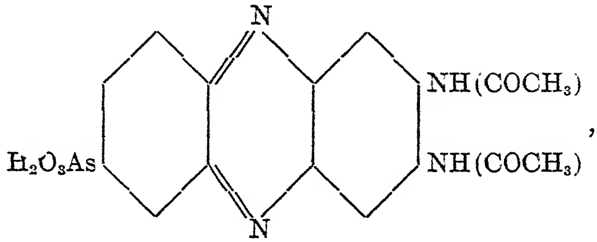
is a brown powder insoluble in alkalis, formed upon diazotizing the preceding compound in acetic acid solution.[1464]

5-Acetylaminothienyl-2-arsonic acid,



crystallizes from water in white prisms, m. p. 134° with decomposition on rapid heating, but unmelted up to 200° with slow heating. It is easily soluble in alcohol, glacial acetic acid or hot water.[102]

2,3-Di(acetylamino)phenazine-7-arsonic acid,

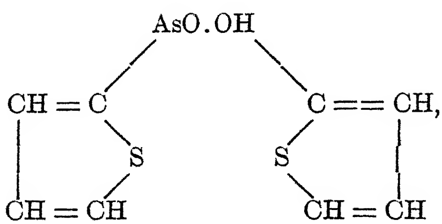


is a yellowish-brown powder soluble in alkalis, resulting upon boiling the corresponding diamino compound with acetic anhydride in acetic acid solution.[1463]

2 or 3-Dimethylaminophenazine-7-arsonic acid may be produced by condensing dimethylaniline with either 3,4-dinitrosophenylarsonic acid or 3-nitro-4-triazophenylarsonic acid. The compound has a blue color, is readily soluble in alcohol, glacial acetic acid or aqueous caustic soda, less so in sodium carbonate, and sparingly in water, ether or benzene.[536]

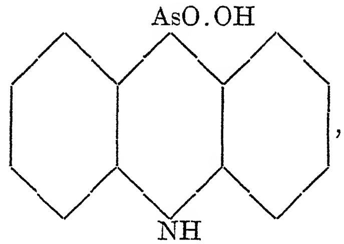
2 or 3-Dimethylaminophenazine-8-arsonic acid, similarly prepared from 2-nitro-3-triazophenylarsonic acid, has a reddish tinge, is readily soluble in alcohol or glacial acetic acid, but insoluble in caustic soda.[1463]

2,2′-Dithienylarsinic acid,



is formed as a by-product in the preparation of thienyl-2-arsonic acid. After the latter has been precipitated as the sodium salt in alcoholic medium, the filtrate is evaporated to dryness, taken up with dilute hydrochloric acid, and the crude arsinic acid recrystallized from hot water. It separates as prismatic needles, m. p. 172°, soluble in alcohol, difficultly so in cold water, and insoluble in ether or benzene.[101]

Phenarsazinic acid,

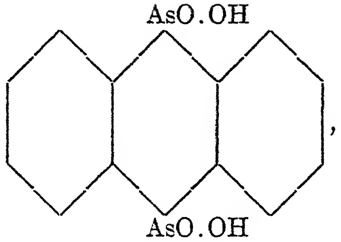


obtained by oxidizing either phenarsazine chloride in glacial acetic acid,[1465] or the corresponding oxide in dilute caustic soda, with perhydrol.[1466] It crystallizes from dilute acetic acid with $1CH_3COOH$ in colorless needles, m. p. above 300°, soluble in dilute alkalis and insoluble in acetone, ether or alcohol. Its colorless sodium salt crystallizes in felt-like needles difficultly soluble in excess of alkali.

γ-Benzophenarsazinic acid, $HN{<}^{C_{10}H_6}_{C_6H_4}{>}As(OH)_3$, results upon oxidizing the corresponding chloride with hydrogen peroxide in glacial acetic acid. It crystallizes from the latter in almost colorless needles remaining unmelted below 260°, soluble in alkalis or glacial acetic acid, and insoluble in the other organic solvents. At 150° it loses $1H_2O$, forming a compound with the usual arsinic acid grouping, $>$ AsO.OH. It sodium salt separates from 95 per cent alcohol as almost colorless, hygroscopic crystals which do not melt below 260°, are soluble in water, alcohol or acetone, and insoluble in benzene or xylene.[1440]

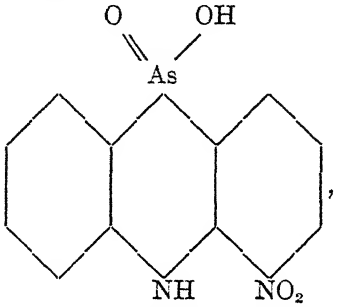
Phenoxarsinic acid, $O{<}^{C_6H_4}_{C_6H_4}{>}AsO.OH$, is derived from the corresponding chloride either by boiling with bromine water or by treating with hydrogen peroxide in glacial acetic acid. It crystallizes in lustrous needles, m. p. 219°, soluble in chloroform, alcohol or hot water. Its sodium salt separates from alcohol-ether in hexagonal plates containing $3H_2O$, not melting below 250°, and soluble in water or alcohol.[1455]

Diphenylene-o-diarsinic acid,



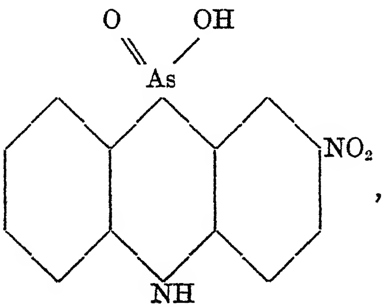
results upon warming the corresponding dichloride with nitric acid (d, 1.38), and subsequently diluting with water. It crystallizes from hot, dilute nitric acid (d, 1.2) in long, colorless prisms which change to a chalk-like powder on washing with water. It melts above 360°, and is very difficultly soluble in all solvents.[1467]

o-Nitrophenarsazinic acid,



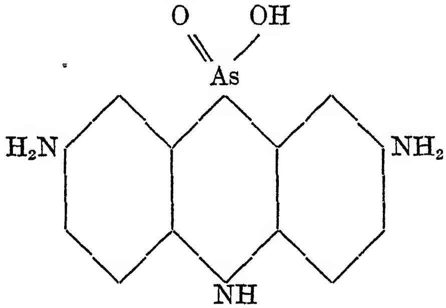
is obtained as pale yellow needles upon nitrating the corresponding acid with fuming nitric acid in glacial acetic acid solution at 16-28°,[1465] or by oxidizing o-nitrophenarsazine chloride with perhydrol in the same solvent.[1468] It crystallizes from dilute acetic acid with $1H_2O$, and from glacial acetic acid with $1CH_3COOH$. Its sodium salt forms brownish-yellow, felted needles.

p-Nitrophenarsazinic acid,



is prepared like the o-isomer, oxidation being avoided by the presence of a slight amount of sulfur dioxide. The acid oxidizes readily in air, especially when dissolved in alkali, with the formation of a violet dyestuff. With ferric chloride it forms a cherry-red solution, from which an amorphous red dye gradually separates, while chromic acid produced first a blue coloration followed by a greenish-black precipitate. Upon the addition of an excess of silver oxide to a neutral solution of the sodium salt, a cherry-red solution of the quinoid compound is produced, from which on evaporation in vacuo the sodium salt separates in lustrous, bronze-colored lamellæ. Upon the addition of mineral acid, the free quinoid acid quickly polymerizes, forming amorphous red flakes.[1472]

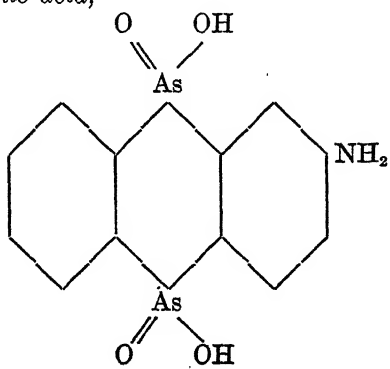
p,p′-Diaminophenarsazinic acid,



,

similarly prepared from the corresponding dinitro acid, is isolated as the dihydrochloride which crystallizes in colorless leaflets. Like the p-amino acid, the aqueous solutions of its alkali salts yield a cherry-red coloration when shaken with silver oxide. On treating an aqueous solution of the dihydrochloride with ferric chloride, there is produced first a deep blue, then a violet coloration, and finally a precipitate of a dark red oxidation product.[1473]

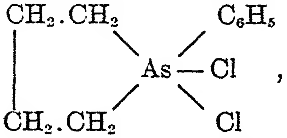
m-Aminoarsanthrenic acid,



,

m. p. 150°, results upon oxidizing the corresponding dichloride with hydrogen peroxide in sodium carbonate solution.[1438]

Phenylcyclotetramethylenearsine dichloride,



prepared by saturating a carbon tetrachloride solution of the corresponding arsine with chlorine, crystallizes in hygroscopic, snow-white crystals, m. p. 120.5°, easily soluble in water or alcohol with decomposition.[1474]

Methylcyclopentamethylenearsine dichloride (Methylarsepidine dichloride), $(CH_2)_5 > As \begin{array}{l} \diagup CH_3 \\ -Cl \\ \diagdown Cl \end{array}$, is derived from the corresponding arsine by treating its aqueous suspension with chlorine. When dried it forms a very hygroscopic, viscous mass which cannot be further purified.[1475]

The corresponding *dibromide* is derived from the arsine by treatment with bromine in carbon tetrachloride solution or with bromine water. When dried it consists of very hygroscopic crystals decomposing in vacuo or upon heating into methyl bromide and arsepidine-bromide.[1431]

The *diiodide,* prepared from its constituents in petroleum-ether, is a yellow, water-soluble powder, m. p. 120° with decomposition. Upon heating its aqueous solution iodine is split off. Silver nitrate precipitates silver iodide with the simultaneous liberation of more or less methyl iodide, depending upon the concentration of the reagent.[1450]

Ethylarsepidine hydroxybromide, $(CH_2)_5 > As \begin{array}{l} \diagup C_2H_5 \\ -OH \\ \diagdown Br \end{array}$, results upon adding cyanogen bromide to ethylarsepidine in commercial ether. It melts at 71°, is easily soluble in water, alcohol, glacial acetic acid or hot nitrobenzene, and insoluble in benzene, toluene or benzine.[1476]

The *cyanobromide,* $(CH_2)_5 > As \begin{array}{l} \diagup C_2H_5 \\ -CN \\ \diagdown Br \end{array}$.—On distilling cyanogen

bromide into an anhydrous petroleum-ether solution of ethyl arsepidine in an atmosphere of carbon dioxide, the addition product separates as a liquid which gradually solidifies. Its melting point could not be determined because it is extremely sensitive to moisture. When gently heated at reduced pressure it decomposes into its components, along with some ethyl bromide and an unidentified reddish-brown to violet crystalline iodo arsenical.[1477]

Phenylcyclopentamethylenearsine dichloride (*Phenylarsepidine dichloride*), $(CH_2)_5 > As\begin{smallmatrix} C_6H_5 \\ Cl \\ Cl \end{smallmatrix}$, from phenylarsepidine and chlorine in dry carbon tetrachloride at low temperature, crystallizes in colorless, hygroscopic prisms or leaflets, m. p. 138-9°, easily soluble in water or alcohol with decomposition. Upon heating up to 150° in an atmosphere of carbon dioxide and then distilling under diminished pressure (20 mm.), decomposition occurs, 1,5-dichloropentane coming over below 200°, while between 200° and 216° there are obtained two unidentified arsenicals, only one of which contains halogen.[1478]

The *dibromide* is an oil.[1452]

The *hydroxybromide* may be obtained either by exposing the cyanobromide to the air, or by dissolving the corresponding dibromide in 96 per cent alcohol and precipitating with ether. It separates in small prisms, m. p. 162.5°, soluble in water, methyl or ethyl alcohol, chloroform, bromoform, carbon tetrachloride, hot acetone or glacial acetic acid, and practically insoluble in ethyl acetate, benzene or ether. It hydrolyzes in aqueous solution with the separation of hydrobromic acid, which may be quantitatively precipitated with silver nitrate but cannot be titrated with 0.1 N-caustic potash solution.[1479]

Phenylarsepidine cyanobromide, a crystalline solid melting at 106-7°, is similarly prepared in ethereal medium. With bromine in an atmosphere of carbon dioxide it yields cyanogen bromide and a yellow oil which gives up its arsenic to alkalis, leaving pentamethylenedibromide. On heating the fused cyanobromide up to 210° in vacuo, it yields a considerable quantity of hydrocyanic acid and a small amount of cyanogen. When heated in an atmosphere of carbon dioxide under reduced pressure in a special apparatus there is obtained a yellow oil of unpleasant odor, b. p. 135-56°/12 mm., which cannot be completely separated into its components.[1480]

The *diiodide* consists of pale yellow crystals, while the *tetraiodide* is a brown oil.[1452]

4-Methylphenylcyclopentamethylenearsine dichloride (p-Tolylarsepidine dichloride), $(CH_2)_5 > As \begin{array}{l} \diagup C_6H_4.CH_3 \\ - Cl \\ \diagdown Cl \end{array}$, prepared like the preceding compound, crystallizes in snow-white needles, m. p. 134°, soluble in alcohol with the formation of the corresponding dihydroxide. It decomposes like the phenyl compound on distilling under diminished pressure.[1453]

Methylarsepidine oxide, $(CH_2)_5 > As \begin{array}{l} \diagup CH_3 \\ \\ \diagdown\!\!\diagdown O \end{array}$, is formed by the direct action of atmospheric oxygen upon the arsine. It consists of small, white needles with a very agreeable aromatic odor, m. p. 150° with decomposition, soluble in alkalis, but insoluble in water.[1450]

Phenylmethylcyclotetramethylenearsonium iodide,

$$(CH_2)_4 > As \begin{array}{l} \diagup C_6H_5 \\ - CH_3 \\ \diagdown I \end{array},$$

from the arsine and methyl iodide, crystallizes from alcohol-ether as a white or faintly yellow crystalline powder, m. p. 135-6°, readily soluble in water or alcohol, but sparingly in ether.[1481]

The corresponding *ethyl* compound is a yellowish powder, m. p. 85-6°; the *n-propyl* derivative crystallizes in fine, white needles, m. p. 123-4°; the *isopropyl* compound is a faintly yellow, crystalline powder, m. p. 113-4° with decomposition, while the n- and *isobutyl* derivatives are non-crystallizable substances. They are all prepared from the arsine and the respective alkyl iodides.

Dimethylcyclopentamethylenearsonium chloride (Dimethylarsepidine chloride), $(CH_2)_5 > As \begin{array}{l} \diagup CH_3 \\ - CH_3 \\ \diagdown Cl \end{array}$, from the corresponding hydroxide and hydrochloric acid, is a black, crystalline, very hygroscopic, water-soluble substance, m. p. 237° with complete decomposition. The *bromide* is a white, slightly hygroscopic solid, m. p. 277-80° with complete

decomposition.[1482] The *iodide,* prepared from the arsine and methyl iodide in ethereal solution, crystallizes from water in colorless, rhombohedric crystals, melting and decomposing at 290°, easily soluble in water or alcohol, and insoluble in ether or ligroin. It yields arsine and pentane with hydriodic acid, a soluble sulfide with hydrogen sulfide, and silver iodide with silver nitrate.[1483] The sulfate, $[(CH_2)_5 > As.(CH_3)_2]_2SO_4$, is a white, hygroscopic solid, decomposing at 232°, and soluble in water. The nitrate is faintly yellow, hygroscopic, melts indefinitely at 260°, and gives up its nitrogen as ammonia when reduced with zinc and sulfuric acid. The acid carbonate is dirty white in color, m. p. 156-7° with decomposition, has a disagreeable odor like methylarsepidine, and is very hygroscopic. It is decomposed by acids with evolution of carbon dioxide, but precipitates the salts of silver and iron like any alkali bicarbonate.[1482] The picrate consists of yellow needles, m. p. 258°, sparingly soluble in water.[1484] The *hydroxide* results upon treating the iodide with moist silver oxide.[1484] Its aqueous solution is strongly alkaline, forms salts with various mineral acids, even carbonic, and has a caustic action upon the skin. It cannot be obtained in solid form as it loses $1H_2O$ upon drying, with the probable formation of the compound $CH_2 = CH.CH_2.CH_2.CH_2.As(CH_3)_2$.

Methylethylcyclopentamethylenearsonium iodide,

$$(CH_2)_5 > As \begin{cases} C_2H_5 \\ CH_3 \\ I \end{cases},$$

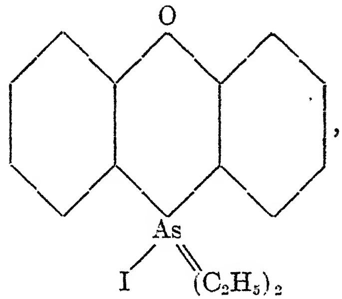
from ethylarsepidine and methyl iodide, melts at 276°, is easily soluble in water, chloroform or hot alcohol, slightly so in cold acetone, and insoluble in ether or benzene.[1485] The corresponding *diethyl* compound resembles the methylethyl derivative both as to method of preparation and properties.[1486]

Phenylmethylcyclopentamethylenearsonium iodide,

$$(CH_2)_5 > As \begin{cases} C_6H_5 \\ CH_3 \\ I \end{cases},$$

prepared from the arsine and methyl iodide, consists of white leaflets, m. p. 179.5°; the *ethyl* compound forms white prisms, m. p. 185°; the *n-propyl* derivative, white crystals, m. p. 137-8°; the *isopropyl* compound, white crystals, while the *n-butyl* derivative consists of white, radiating crystals, m. p. 140°.[1487]

Diethylphenoxarsonium iodide,



results upon refluxing As-ethylphenoxarsine with the calculated amount of ethyl iodide. It crystallizes in pure white, translucent needles not melting below 300°.[1488]

Chapter VII. Miscellaneous Arsenicals.

1. *Protein Combinations Containing Arsenic.*—Albumin from egg-white is treated successively with phosphorus pentoxide and arsenic trichloride, allowed to stand for some time, the excess of inorganic reagents decomposed with water, and the resulting phosphoric and arsenious acids removed by washing with water. The product is a brown, amorphous mass insoluble in water, dilute acid or organic solvents, but easily soluble in dilute alkalis. It does not give the usual tests for arsenic with hydrogen sulfide or ammonium phosphomolybdate.

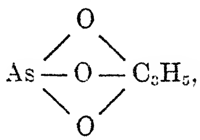
By gradually adding sulfur trioxide to egg-white at low temperature, allowing the mixture to react with arsenic trichloride, and finally washing free of inorganic acids with water, a yellowish-brown, amorphous powder is obtained which is insoluble in water, dilute acids, alcohol, ether, chloroform, benzene, toluene or other organic solvents, but dissolves easily in dilute alkalis, and in concentrated acetic or lactic acid after prolonged digestion. Its alkaline solution is not coagulated on warming.[1489] Similar compounds have been obtained from casein, plant-albumin, peptones and albumoses, the arsenic being so firmly combined that it does not respond to the ordinary qualitative tests.[1490]

An arsenical compound results on adding an alcoholic solution of arsenic trichloride to a suspension of gliadine or glutenine in the same reagent and stirring for six hours. By distilling off the solvent in vacuo, pulverizing the residue, washing with 99 per cent alcohol and drying in vacuo, the product is isolated as a brownish powder soluble in hot water, in which, by continued boiling, the arsenic is split off and can be identified by the usual reagents. The product is also soluble in aqueous sodium hydroxide or carbonate, partially in ammonia, and completely in concentrated acids with partial decomposition. It gives the biuret reaction, and is insoluble in the stomach juices, the arsenic being gradually split off while the protein is digested.[1491]

Arsenic derivatives may also be obtained by warming phosphatides dissolved in organic solvents with arsenic acid. It is not necessary to employ pure phosphatides, as materials containing them or extracts of the same yield similar results. The products still retain the properties of phosphatides—they are soluble in ether, fats or oils and may be emulsified. Such compounds have been obtained from lecithin, lecithin-albumin, ground oats or brain substance.[1492]

On adding sodium cacodylate to a solution of nucleinic acid in aqueous sodium phenate and evaporating to dryness, a pale yellow

powder is obtained which crystallizes from hot water in needles soluble in aqueous alkalis, and decomposing above 180°.[1493]

2. *Arsenicals without C — As Linkage.*—Alkyl and aryl arsenites have been prepared by refluxing crystallized arsenic trioxide with various alcohols or phenols in the presence of either calcium carbide[1494] or anhydrous copper sulfate[1495] as dehydrating agents. The aliphatic compounds also result upon refluxing arsenic trihalides and sodium alcoholates.[1496] Thus, there have been prepared the *methyl, ethyl, propyl, isobutyl, trimethylcarbinyl, amyl, isoamyl, phenyl, o, m, and p-tolyl- benzyl, β-naphthyl and resorcyl arsenites.* The ethyl ester may also be produced by heating arsenic trioxide and ethyl silicate in a sealed tube at 200°, or from ethyl iodide and disilver arsenite at 150°. A *glyceryl derivative,*  is derived from the corresponding acetyl compound and glycerine.[1497] With the exception of the β-naphthyl compound, they are all liquids generally soluble in methyl or ethyl alcohol, ether, benzene, chloroform or ethyl acetate, and readily hydrolyzed by water, yielding arsenic trioxide.

Acetyl arsenite, $As(O.COCH_3)_3$, from arsenic trioxide and hot acetic anhydride, consists of white needles, m. p. 82°; b. p. 165-70°/31 mm.; easily soluble in chloroform or ethyl acetate, sparingly in cold benzene or carbon tetrachloride and practically insoluble in petroleum ether or carbon bisulfide. It is readily decomposed into acetic acid and arsenic trioxide by water or alcohols in the cold. When fused with benzoic acid, it yields the corresponding *benzoyl derivative,* $As(O.COC_6H_5)_3$, a white, crystalline mass, m. p. 155°; easily soluble in chloroform, less so in benzene or ethyl acetate and difficultly in carbon bisulfide, carbon tetrachloride or petroleum ether. It is easily decomposed by moist air.[1498]

Methyl and *ethyl arsenates* have been prepared from dry silver arsenate and the respective alkyl iodide at 100°. They are both liquids, the methyl ester boiling at 128-30°/60 mm., and the ethyl ester at 148-50°/60 mm. Their densities are 1.5591/14.5°, and 1.3264/0° respectively.[1499]

Dibromobehenic acid yields an ester on warming with silver arsenate at 125-70°, while bromolecithin yields a similar compound in boiling toluene.[1500]

A complex ester, $O = As(OC_6H_2I.OH.SO_3Na)_3$, results upon heating silver arsenate with aqueous sodium 2,6-diiodophenol-4-sulfonate at 100°.[1500]

Hexamethylenetetraamino arsenate, $(C_6H_{12}N_4)_3.(H_3AsO_4)_2$, is precipitated on mixing its components in alcoholic solution.[1501]

Tri(methylamine) dithioarsenate, prepared from methylamine hydrochloride and trisodium dithioarsenate, consists of white needles containing water of crystallization. The corresponding ethylamine and organic ammonium salts may be similarly obtained.[1502]

Trianiline-arsine hydrochloride, $\left(C_6H_5.N\begin{matrix} \diagup H \\ -H \\ \diagdown Cl \end{matrix}\right)_3 \equiv As$, is produced by the gradual addition of aniline to a cold heptane solution of arsenic trichloride, and purifying the crude product by sublimation. The compound is a light yellow, crystalline solid melting at 148-50° with slight decomposition, and insoluble in the common inert solvents. It is unstable, decomposing readily in hot water or absolute alcohol and oxidizing on exposure to air.[1503]

Mono aniline arsenate, $C_6H_5.NH_3.O.As\begin{matrix} /\!\!/ O \\ \diagdown (OH)_2 \end{matrix}$ results upon adding an excess of syrupy arsenic acid to an alcoholic solution of aniline. It crystallizes in pearly leaflets, m. p. 147-8°.[1466]

The corresponding *dianiline* salt is similarly obtained by adding an excess of aniline to an alcoholic solution of syrupy arsenic acid. It crystallizes in pearly leaflets, m. p. 143°.[1504]

Tripyrocatecholarsenic acid, $\begin{matrix} HO.C_6H_4.O \diagdown \\ HO.C_6H_4.O - \\ HO.C_6H_4.O \diagup \end{matrix} As = O.4H_2O$, formed on mixing arsenic and pyrocatechol in hot aqueous solution, separates in efflorescent plates, m. p. 103°; soluble in water, methyl or ethyl alcohol, ether, acetone or glacial acetic acid, slightly so in chloroform, and insoluble in benzene. It hydrolyzes in dilute aqueous solution, especially on heating or upon the addition of acids. The compound is unaffected by diffused daylight, but turns greenish-black in direct sunlight. Its concentrated aqueous solutions form crystalline salts with ammonia or alkali hydroxides, as well as with salts of the alkali, alkaline earth or bivalent heavy metals. The alkali and ammonium salts may also be obtained from hot concentrated solutions of primary arsenates and pyrocatechol, but not from arsenates containing more than one equivalent of alkali. There have been prepared lithium, ammonium,

potassium, sodium, calcium, barium, magnesium, zinc, ferrous, nickel, cobalt, manganese, chromic, aluminium, mercurous, silver, thallium, cerium, lanthanum, yttrium, hexamminecobaltic, aquopentamminecobaltic, chloropentamminecobaltic, aquopentamminenickel, mono- and dipyridine, monoquinoline, mono- and dianiline, and guanidine salts. Various alkaloids (morphine, quinine, strychnine, colchicine, hydrastinine, veratrine, coniine, apomorphine) as well as dilute peptone or albumin solutions form precipitates with the acid, some even at very great dilutions.

The tetrahydrated acid may be converted into the dihydrate either by adding concentrated hydrochloric acid to its concentrated solution, or by crystallizing it from glacial acetic acid. The tetrahydrate is converted into a dimethyl or diethyl alcoholate by recrystallization from the respective alcohol.[1505]

Pyrogallolarsenic acid, $[(HO)_2C_6H_3.O]_3AsO$, is made by condensing pyrogallol and arsenic acid.[1506]

Iron salts of *arsenitartaric* and *arsenicitric acid* have been prepared either by treating the corresponding alkali salts with iron salts; from iron tartrate or citrate and arsenic acid; or from tartaric or citric acid and iron arsenate. The acid ferrous arsenitartrate is a grayish-white powder soluble in cold dilute caustic soda or ammonia; the acid ferrous arsenicitrate is a green powder; the acid ferric arsenitartrate consists of yellow crystals soluble in alkalis; the acid ferric arsenicitrate is a yellowish-green crystalline substance; the neutral sodium ferric arsenitartrate consists of deep yellow crystals insoluble in alcohol.[1507]

Quinoline, tetrahydroquinoline and 8-hydroxyquinoline combine additively with arsenic trichloride in ethyl acetate solution, forming the compounds $C_9H_7N.AsCl_3$, m. p. 138°; $C_9H_{11}N.AsCl_3$, m. p. 134°; and $C_9H_7NO.AsCl_3$, m. p. 168°, respectively. Both quinoline and tetrahydroquinoline react with one molecular equivalent of arsenic acid to form the arsenates $C_9H_7N.H_3AsO_4$ and $C_9H_{11}N.H_3AsO_4$ respectively.[1508]

Appendix I. The Chemotherapy of Organic Arsenicals.

A. General

The comparatively new science of chemotherapy has within the past two decades become an important branch of medicine. It has not only contributed very useful drugs for the treatment of disease, but has also enriched medical knowledge with valuable theories, and has assisted in the development of some of the most fruitful ideas regarding the relationship between chemical constitution and biological effect.

To Ehrlich must be attributed the development of some of the most important theoretical conceptions and fundamental principles of chemotherapy, such as the theories regarding the parasitotropism and organotropism of chemotherapeutic agents, and the conception of specific chemical receptors, the latter being based upon the discovery of the specific drug resistance of various parasites. In seeking an explanation of the manner in which (1) quinine causes malaria parasites to disappear from the blood; (2) mercury favorably influences syphilitic manifestations, and (3) organic arsenicals destroy various trypanosomes and spirillæ, Ehrlich came to the conclusion that these results were due to the fact that parasites combine with the chemical in question. In other words, there exists between the parasites and the drugs a certain specific chemical affinity to which he applied the term parasitotropism. This can be easily demonstrated either by the diminution of the movements of various motile parasites when brought in contact with certain chemicals under the microscope, or by similarly treating the microörganisms in a test tube, subculturing, and then observing the diminution of growth or its complete cessation. The destruction of microörganisms in the animal body is much more difficult, as all sterilizing agents are not only toxic toward the protoplasm of the bacteria but also toward the cells of the host, the latter property being known as organotropism. The value of a chemotherapeutic agent is, therefore, based on the relationship between its parasitotropism and organotropism. Thus, if a quantity of a mercurial compound, sufficient to destroy a certain number of a definite organism in the test tube, is injected into an animal containing the same number of parasites, we find that very little effect is produced because the mercurial acts upon the host rather than upon the parasite, i.e., its organotropism completely eclipses its parasitotropism. Therefore, only such chemical compounds can be considered as therapeutic agents which

have a great effect upon parasites, but only a slight action upon the animal body.

When a mouse infected with trypanosomes is treated with parafuchsin or tryparosan (chlorinated parafuchsin) the parasites first disappear from the blood but reappear after several weeks. A second injection of parafuchsin causes the above phenomenon to be repeated; upon continuing the same experiment the action of the successive additions of fuchsin gradually becomes weaker until it finally fails to exert any influence upon the microörganisms, due to the resistance against fuchsin acquired by the parasites. This resistance is retained even upon transferring the parasite into another animal. In a similar manner there have been obtained atoxyl-fast strains which cannot be destroyed by atoxyl even after 400 passages through normal animals. These strains are also resistant toward phenylarsonic acid, but not toward triphenylmethane dyes. It has also been demonstrated that trypanosomes, which have acquired a resistance against organic arsenical compounds containing pentavalent arsenic, can still be readily influenced by those with trivalent arsenic, although resistance against the latter can also be developed in the above manner. To explain these phenomena, Ehrlich suggested the idea that the protoplasm of the cells of microorganisms contains various groupings (chemical receptors) which are able to combine with definite chemical radicals. Accordingly, upon treating trypanosomes with arsonic acids only the arsonoceptor is affected, while upon further treatment with an arseno compound, e.g., arsenophenylglycine, the arsenoceptor and aceticoceptor are also affected.

In the field of practical therapy Ehrlich distinguished between the gradual and the immediate elimination of organisms from the body. In the first case the patient is treated over an extended period of time with successive quantities of the drug, each quantity being insufficient to completely destroy all of the parasites. This method, utilized by Koch in the treatment of sleeping sickness with atoxyl, is employed in the treatment of malaria and also in the therapy of syphilis by mercurials. According to the second procedure, "therapia sterilisans magna," complete sterilization and permanent cure is effected by a single large dose of the chemotherapeutic agent. Despite the fact that Ehrlich claimed to have achieved such remarkable results in the treatment of experimental trypanosomiasis with arsenophenylglycine, the second method often involves various dangers and difficulties, and has therefore not been found practical in human therapy. More recently there has been developed a third procedure which consists in introducing two or more medicaments by different routes. Thus, in human syphilis the most satisfactory results have been obtained by employing intravenous injections of arsphenamine or neoarsphenamine in conjunction with inunctions of various mercurials, while cures in rabbits infected with

trypanosomes have been effected by a small dose of arsenophenylglycine injected intravenously and a large amount of tryparosan administered orally.

In determining the chemotherapeutic value of a substance in diseases caused by pathogenic microörganisms a complete study of its biological, clinical and chemical properties is necessary so that some relationship may be established between them and the chemical constitution of the compound. The biological studies consist of the determination of the toxicity and therapeutic value, both of which are carried out with experimental animals. The toxicity may be established in several ways. Some experimenters introduce the drug into the animal through the mouth, while others employ subcutaneous, intramuscular or intravenous injections of an aqueous solution of definite concentration, noting the resulting metabolic disturbances or organic injuries. A shorter and at the same time more accurate method consists in establishing the minimum lethal dose, i.e., the minimum amount necessary to kill the animal and the maximum dose tolerated without causing death during a definite period (usually 7 to 10 days), both values being expressed in terms of milligrams per kilogram of body weight.

Technic of Toxicity Tests.—It is now well known that in testing the toxicity of drugs by intravenous administration, the results may be modified by various factors, such as the degree of concentration of the solution, the rate of injection, etc. For comparative tests the technic must be uniform, the method employed being preferably the one standardized by the Hygienic Laboratory at Washington, D. C., which may be briefly described as follows:

Healthy, non-pregnant, white rats weighing between 100 and 150 g. and kept under observation for at least ten to fourteen days before being used in these tests, are reweighed before injection, and the dose administered in proportion to the body weight. All animals are fed late in the afternoon of the previous day in order that the weights may be taken and the injections made after a period of about eighteen hours' fasting, to render the dosage more accurate. The injection is made by the gravity method, employing a special apparatus, Fig. 2.

This is composed of a 2 c.c. burette A divided into 0.01 c.c. and fitted with a two-way cock at the upper end B for filling by means of suction by vacuum C, and a water-tight cock at the lower end D for stopping the injection. The opening at E admits air to the pipette during the injection when the cock at B is turned after filling the pipette with solution, to cut off the vacuum. A long glass nozzle F is attached to the burette fitted with a short piece of the best grade rubber tubing G carrying a window near the end, and a needle H of No. 26 to No. 22 gauge.

Before injecting the solution, the needle and rubber tubing are sterilized by boiling, and the burette cleansed by copious flushing by means of the vacuum suction with sterile water, followed by the solution

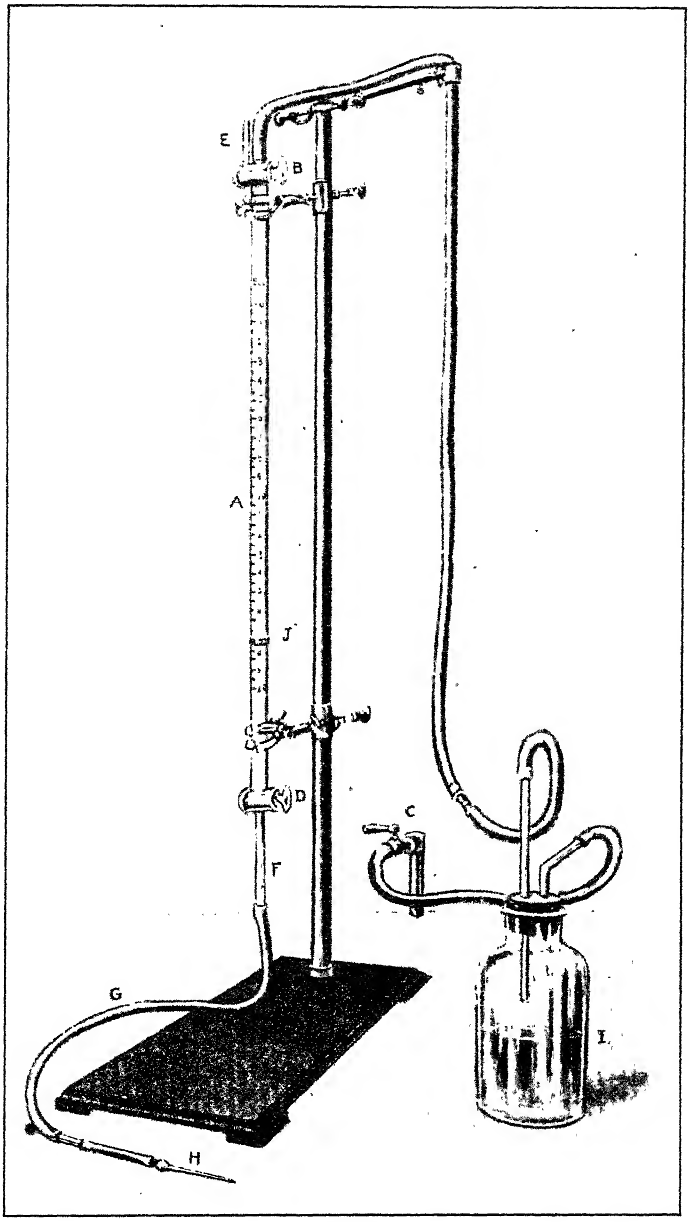


FIG. 2

to be injected, and are collected in the bottle I interposed between the vacuum and the burette. When solutions are changed the apparatus is cleansed in the same manner.

After the animal is bound upon the operating board, the skin of the anterior surface of the thigh is cleansed with alcohol and a small incision made over the saphenous vein, which is rendered prominent by pressure made in the inguinal region by an assistant. The vein is grasped with fine forceps, due care being taken not to produce pain by grasping the nerve alongside of it, the needle is inserted, and the cock D gradually opened to regulate the flow while the time in seconds is called off by an assistant, until the dose to be given, previously marked off by the rider J fastened to the burette, is injected.

With this apparatus it is possible to inject a given amount of solution very accurately and at a given rate of flow, the speed set down by the Hygienic Laboratory being 0.5 c.c. per sixty seconds. The amount of solution to be injected is calculated according to the dose to be given per 100 g. of weight, and the rate of injection can be nicely regulated by means of the stop cock at D and timed with a stop clock. The apparatus is to be recommended for the intravenous injection of rats, guinea-pigs and rabbits.

Subcutaneous and intramuscular injections of drugs are often very irritating to the skin and muscles of the animal, and the results are seldom as sharp and clear cut as those following intravenous injections. In conducting therapeutic tests, the selection of the infectious microorganisms is of the utmost importance, for upon it depends to a great measure the length of the experiment, the accuracy of the comparative evaluation of the remedy and the proper interpretation of experimental findings in relation to the treatment of human infection. Thus, Trypanosoma lewisi which does not kill the animal, cannot be satisfactorily employed experimentally, as no idea can be gained as to the ability of a drug to prolong the life of the infected animal. Similar inconclusive results are obtained with Spirocheta recurrentis, the parasite of relapsing fever, on account of the frequent remissions and the disappearance of the parasite from the peripheral blood even without the assistance of chemotherapeutic agents. The microörganism of chicken spirillosis has been frequently employed as a test parasite, but it is so easily influenced by various chemicals that it does not serve as an ideal means of distinguishing between drugs of high and low efficiency. Treponema pallidum, the spirochete of human syphilis, is not well adapted for animal experiments, as the disease produced takes a mild form and is chronic in character, necessitating observations for about four to six months. This not only causes great delay, but also renders the experiments very expensive on account of the housing and feeding of the numerous animals. Despite these disadvantages, however, the chemotherapeutic investigation of so called "rabbit syphilis" is beginning to be employed very

extensively. The work of Ehrlich and Hata,[1509] Kolle and his collaborators, Nichols,[1510] Brown and Pearce[1572] and others have thrown so much light on the course of the Treponema pallidum infection in rabbits, that it is now possible to determine the curative dose with a fair degree of accuracy, or at least to draw a definite comparison between the activity of various drugs. In some industrial laboratories arsphenamine and neoarsphenamine are frequently tested by this method as a control upon the results obtained in the routine therapeutic tests with other parasites more readily adapted for daily use.

The rabbits are usually inoculated in both testicles with an emulsion containing spirochetes, and the latter allowed to multiply for about two weeks, when the testicles become considerably enlarged and indurated, a marked infiltration being observed at the points of inoculation. The drug is now injected intravenously or intramuscularly, and if it reacts favorably, the regression of lesions proceeds rapidly, resulting in complete resolution by the end of seven to fourteen days. If the dose of the drug is too small, or if the compound is not very efficient, residual lesions in the form of diffuse thickenings or circumscribed nodules may still be seen. With a sufficient amount of the proper drug, however, no reinduration takes place for many months, and the animal is finally pronounced cured if at the expiration of six months no spirochetes can be found in the testicles.

Ehrlich and his co-workers used various strains of trypanosomes as test parasites for determining the therapeutic activity of organic arsenicals, and obtained highly satisfactory results. They found that the destructive action of the arsenicals varies with different types of trypanosomes: Trypanosoma brucei (the parasite of Nagana disease of horses) is destroyed with difficulty by arsphenamine or neoarsphenamine, while Trypanosoma equiperdum is more easily influenced. Schamberg, Kolmer and Raiziss[1592] suggested Trypanosoma equiperdum as the test parasite for the routine testing of organic arsenical compounds, particularly those of the arsphenamine group. The inoculation of white rats with definite numbers of this trypanosome can be made with such precision, that the infections produced are definite and uniform, the evidence of therapeutic activity is sharp and decisive, and the period of observation required is not longer than two or three weeks. The assumption that there exists a close relationship between the results obtained with T. equiperdum in experimental animals and those observed clinically with T. pallidum has been confirmed by Schamberg, Kolmer and Raiziss,[1592] and also by Voegtlin and Miller,[1511] who found that compounds possessing a high or low efficiency in one of the above infections behaved similarly with the other. The value of trypanocidal tests is, however, sharply limited, inasmuch as certain other medicinals of value in the treatment of pallida infections, notably the mercurials,[1512] are unable to influence the course of experimental trypanosomiasis, due in part to their high

toxicity which prevents the administration of sufficiently large doses. These tests may, therefore, be regarded as indicators of the comparative therapeutic value of drugs possessing trypanocidal activity in vivo; medicinals such as the mercurials or bismuth compounds, however, which fail to influence experimental trypanosomiasis, may still possess spirocheticidal properties.

As stated by Pearce and Brown,[1513] the treatment of experimental trypanosomiasis of mice and rats is largely a matter of speed of action, yielding valuable data regarding the therapeutic activity of a compound in a relatively short time. These investigators, however, have very properly indicated that experiments of this character do not involve the treatment of chronic tissue changes, as in trypanosomiasis of guinea-pigs and rabbits, which are more nearly analogous to the naturally acquired forms of the disease, but that the two types of infection supplement each other in the chemotherapy of experimental trypanosomiasis.

Technic of Trypanocidal Tests.—The T. equiperdum appears in the peripheral blood (tail) within forty-eight to seventy-two hours after intraperitoneal infection; by the fifth to seventh day after infection enormous numbers of trypanosomes are to be found in the blood and may even outnumber the erythrocytes, the untreated animals usually dying at this stage.

The question of infection is very important in relation to the results of these tests. A satisfactory procedure consists in infecting the animal twenty-four hours before the injection of the drug. Now Kolmer[1514] has shown that the number of trypanosomes used in the infection greatly influences the results, a great number of the parasites requiring a much larger dose of the chemical for sterilization than a smaller number. In this connection the Kolmer method of counting the trypanosomes and infecting with approximately known numbers with blood removed asceptically from the heart of the seed animal[1515] has proved itself to be of distinct value. It is only by using rats of approximately the same weight and infecting with approximately known numbers of trypanosomes by intraperitoneal injection that the experiments are rendered uniform and comparative.[1516] The dose is prepared separately for each rat in small sterile vials, and is contained in 1 c.c. which is slowly injected with a syringe in a saphenous vein. The blood of each animal, including the controls, is examined each day over a period of three weeks by placing a drop from the tail on a cover-glass and allowing it to spread in a film when placed upon a slide.

A shorter yet accurate method has been proposed by Voegtlin and Miller,[1511] in which the final results are read twenty-four hours after the injection of the drug. The principle of the method is based on the fact that a well-defined dose of the drug is required to kill a certain number of parasites in the blood of infected rats, i.e., the parasiticidal power of the drug is measured in terms of the number of parasites killed.

Technic of Test.—Healthy albino rats from one breeding strain and weighing about 50 to 60 grams are put on a diet of milk, bread and oats until they reach a weight of 100 to 150 grams, when they are ready to be used for the test. A series of non-pregnant animals is inoculated with citrated blood from a seed rat. The latter, showing about 200,000 trypanosomes per cubic millimeter of blood, is bled by decapitation directly into 5 c.c. of saline solution containing 2 per cent of sodium citrate, and about 0.5 c.c. of the resulting suspension of parasites is injected intraperitoneally into each rat. The above amount of the suspension will usually produce in 24 hours an infection of about 100,000 parasites per cubic millimeter of blood, and if left untreated the animals will die, as a rule, two days later.

The injection of the drug to be tested is carried out as follows: The drug is dissolved in distilled water, and the concentration adjusted in such a way that the volume of the desired dose is within from 0.3 to 0.9 c.c. An accurately calibrated tuberculin syringe, provided with a 26-gauge Luer needle, is then filled with the freshly prepared solution, and the drug immediately injected at a slow rate into the leg vein previously exposed by skin incision. The number of trypanosomes per cubic millimeter of blood should be within 100,000 to 250,000, preferably 100,000 to 150,000, for, as Voegtlin and Smith [1517] have shown and subsequent experience has confirmed, the choice of a uniform grade of infection is very important for accurate work.

This procedure is about to be adopted by the United States Public Health Service as a control test for the trypanocidal efficiency of various lots of arsphenamine and neoarsphenamine. Graded doses of the drug are injected into a series of animals. It has been found that a variation of approximately 50 per cent between successive doses (1, 1.5, 2.25, 3.75, 5, 7.5, 10, etc.) is all that can be expected of the accuracy of the test. This is due to the fact that quantitative differences in the metabolism of the drugs and the rate of excretion of the arsenic in different rats are sufficiently great to produce considerable variations in parasiticidal action. These variations make it necessary to test at least five rats at each dose. At the end of 24 hours after the injection of the drug, the number of parasites in the tail blood is again determined, first by a preliminary examination of a drop for the presence or absence of parasites, and then by a count of the blood specimens which were found positive in the preliminary examination. The method permits an accurate count of 1,000 or more parasites per cubic millimeter; below 1,000 the count is unreliable. The dose required to bring the parasitic count within 24 hours to a trace or negative, or, in other words, the dose which kills from 100,000 to 250,000 parasites per cubic millimeter of blood, is called the minimum effective dose. As a rule the blood is again examined at the end of 48 and 72 hours after treatment.

From the foregoing it can be seen that in order to compare the chemo-

therapeutic value of various drugs, determinations of the toxic and the therapeutic or curative doses must be made upon the same species of animals and with the same parasite. In expressing comparative toxicity results it is necessary to state the animal employed as well as the method of administration of the drug; whether intravenously, intramuscularly, subcutaneously or orally. The virulence of an infectious microörganism is controlled by the effect of a drug selected as a standard. Arsphenamine is often employed in the latter capacity as it yields comparatively constant results with each type of microörganism.

Recently a new term, chemotherapeutic index, has been adopted in the field of chemotherapy. It is the value obtained by dividing the maximum tolerated dose M. T. D. by the minimum curative dose M. C. D., and is expressed by the equation:

$$\text{Chemotherapeutic index I} = \frac{\text{M.T.D.}}{\text{M.C.D.}}$$

By comparing the figures thus obtained for different compounds under the same experimental conditions, there is afforded a ready means of noting the comparative efficiencies of various drugs. Thus, if the chemotherapeutic index of a substance X is 40 and that of another compound Y is 50, then the latter is 1¼ times more efficient with the particular infection employed.

The problem most vital to the science of chemotherapy is the establishment of a relationship between the chemical constitution of a substance on the one hand and its chemotherapeutic index on the other, for once the influence of various radicals upon parasites or upon the animal body is definitely determined, the synthesis of new compounds will assume a more rational course.

The first investigations along these lines were carried out by Ehrlich. He found that by producing various changes in the molecule of p-arsanilic acid there were produced a number of compounds, the toxicities of which were different from that of the parent substance. When employed in therapeutic experiments, however, they proved to be of little or no value. Favorable results are obtained upon introducing an acetyl radical into the amino group of arsanilic acid; the curative power of the acetyl derivative equals that of atoxyl, but in addition is three to ten times less toxic. Upon continuing his investigations Ehrlich observed that although atoxyl and arsacetin, even in minute amounts, were trypanocidal in the animal body, they failed to destroy the same organisms in the test tube in concentrations as high as 2 per cent. To explain this phenomenon, he assumed that in the animal body the pentavalent arsenic is first reduced to the trivalent condition before action upon the infectious microörganisms begins. This assumption was subsequently substantiated by a study of two trivalent arsenical derivatives of p-arsanilic acid: 4-aminophenylarsine-oxide and 4,4′-diaminoarseno-

benzene. This led to the discovery of the remarkable trypanocidal and spirillicidal effects of the arseno group (—As = As—). That the nature of the radical present in the nucleus of phenylarsonic acid has a vital influence upon its toxic action may be seen in the following table, showing the dilutions at which 1 c.c. of the various derivatives will kill a mouse weighing 20 g.

	Sodium salt	*AsO Derivative*	*As = As Derivative*
$H_2O_3AsC_6H_4NH_2$	1:200	1:15,000	1:6,000
$H_2O_3AsC_6H_4OH$	1:75	1:13,000	1:1,000
$H_2O_3AsC_6H_4NHCH_2COOH$	1:20	1:1,000	1:70

The trivalent arsenicals are also more trypanocidal than the pentavalent compounds in the test tube, as may be seen in the following example: 4-hydroxyphenylarsonic acid does not kill trypanosomes in dilutions of 1 to 2 per cent, while the corresponding arsineoxide, in a dilution of 1:10,000,000, produces sterilization in one hour. Similar results are obtained in vivo: 1 c.c. of a 1:40,000 solution of 4-hydroxyphenylarsine-oxide causes an immediate disappearance of trypanosomes from an infected mouse, the animal remaining entirely free of parasites for seven days.

The same investigator later found that in therapeutically effective benzene derivatives containing two different pharmacodynamic substituents, one of which is a salt-forming group (OH, NH_2, etc.), the introduction of a third substituent in ortho position to the salt-forming group would necessarily increase the activity of the compound. This was deduced from studies with Trypan-blue, parafuchsin, Trypan-red and its homologues. Thus, in the case of p-arsanilic acid he found that its activity was increased by the introduction of halogens in the ortho position to the amino radical. Such substituents are said to have a eutherapeutic action. On the other hand, the introduction of a methyl or nitro group ortho to the amino radical in the above arsonic acid decreases the activity of the parent compound, in other words, they have a distherapeutic effect. By introducing iodine into 4,4′-dihydroxy-arsenobenzene, however, the trypanocidal action in experimental animals completely disappears, while the spirillicidal power is greatly increased. Finally, after experimentation with various groups, Ehrlich observed that the most striking results were obtained with 3,3′-diamino-4,4′-dihydroxyarsenobenzene (arsphenamine base), the dihydrochloride of which has since become one of the leading medicaments in the treatment of syphilis.

It is interesting to note that the introduction of two additional amino groups into arsphenamine, as in 3,5,3′,5′-tetraamino-4,4′-dihydroxyarsenobenzene, increases the toxicity of the parent substance 39 per cent, while the therapeutic dose remains the same. Numerous N-substituted derivatives of arsphenamine have also been studied, and

the following figures will serve to indicate the significance of the amino group in arsphenamine. Neoarsphenamine, a derivative of 3,3′-diamino-4,4′-dihydroxyarsenobenzene, containing a sodium methylenesulfinate group attached to one and also part of the second amino radical, has a maximum tolerated dose of 254 mg. (approximately equivalent to 50 mg. of elemental arsenic) per kilogram of body weight, while that of arsphenamine is 100 mg. (approximately equivalent to 30 mg. of arsenic). Here it is evident that the substitution in the amino group results in a reduction in toxicity amounting to about 40 per cent. The minimum therapeutic dose, however, is increased from 23 mg. in the case of arsphenamine to 40 mg. in the case of the neo compound, amounting to 16 per cent. Furthermore, by introducing various fatty acid groups into both amino radicals of arsphenamine, forming compounds of the type

$$(HOOCCH_2.HN)(HO)C_6H_3As=AsC_6H_3(OH)(NH.CH_2COOH),$$

the toxicity and therapeutic effects are lowered. From the preceding illustrations it is evident that a change in the chemical constitution of a compound affects its chemotherapeutic properties, but as yet no definite laws regarding this important subject have been established.

B. Special

Chemotherapeutic experiments with animals often yield varying results; in the hands of different investigators the same compound may in many cases fail to act uniformly, chiefly on account of the individual susceptibility of the experimental animals, the technic and conditions of the experiment, and the virulence of the strain of parasites employed. Clinical observations are even less uniform because of the difficulties involved in standardizing the methods of treatment, the individual idiosyncrasy of the patients, the interference of other medication, and the lack of strict coöperation on the part of the patients. Another cause of discrepancies in both clinical and experimental investigations may be frequently attributed to some impurity in the drug; in many cases, e.g., arsphenamine and allied arsenicals, no methods of obtaining chemically pure products have been developed. This is of vital importance as the slightest trace of impurity often has an enormous influence upon the toxic action of the compound. Hence, chemotherapeutic results can only be properly evaluated when all the conditions of the experiment are mentioned; in most cases the figures obtained are of value merely for purposes of comparison. In the following pages are indicated the results obtained with some of the more important organic arsenic compounds which have appeared in the literature.

Inorganic arsenic compounds have been employed in the therapy of various diseases for many years, but their high toxicity has prevented

them from finding extended practical application. Thus, the maximum tolerated dose (M. T. D.) of sodium arsenite injected intravenously into white rats is 3 mg. per kg. of body weight, while that of sodium arsenate is 50 mg. per kg. Furthermore, sodium arsenite does not influence trypanosomes in doses of 3 mg. per kg.; the same is true of sodium arsenate in doses of 30 mg. per kg.[1526]. According to Voegtlin and Smith, however, the M. T. D. for sodium arsenite is 7.89 mg. per kg.; its minimum lethal dose (M. L. D.) 11.05 mg.; and minimum effective dose (M. E. D.) in Trypanosoma equiperdum infection, 11.05 mg. With sodium arsenate the M. T. D. is 72.8 mg.; the M. L. D. 104 mg., and the M. E. D. 78 mg. per kg.[1527]

Disodium ethylarsonate ("**Monarsone**") is tolerated in doses of 200 mg. per kg. but in experimental trypanosomiasis it is ineffective in doses approaching the maximum tolerated dose.[1526] Nichols of the U. S. Army Medical School found that the same compound has no effect on Spirocheta pallida.[1528]

Cacodylic acid, in the form of its sodium salt, has been employed in medicine for many years, and is still used intravenously in the treatment of certain skin diseases, malaria and secondary anemias. As early as 1843 the above acid was found by Bunsen to be comparatively non-toxic for frogs even in large doses. This he attributed to the fact that the arsenic is combined in a different manner than in the inorganic compounds.[12] Subsequent investigations, however, have shown that, like other arsenicals, it produces pathological changes in the animal body, and in cases of lethal intoxication the post-mortem findings show that the effects are analogous to those of arsenic poisoning. In proportion to its arsenic content, cacodylic acid is less toxic than arsenious acid.[1529] When introduced into the body it is largely eliminated unchanged in the urine, the remaining portion being almost entirely reduced in the stomach, intestines and liver to the corresponding arsineoxide, and is exhaled as such. A small fraction of the cacodylic acid is also converted into arsenious and arsenic acids which are ultimately found in the urine.[1530]

Tetramethylarsonium iodide.—Bürgi[1531] found that this compound exerts a paralyzing influence on the central nervous system but does not affect the heart of a frog or rabbit. It is not decomposed in the animal body, the greater part being eliminated in the urine.

Tetraethylarsonium iodide behaves like the corresponding methyl compound except that its action upon the central nervous system is about four times as strong.[1532]

3-Amino-4-hydroxyphenylarsineoxide (Arsenoxide), injected intravenously in the form of a 2 per cent solution of its hydrochloride, produces a rise in the pulmonary pressure of dogs similar to that caused by a 2 per cent solution of unalkalinized arsphenamine. The M. L. D. of its sodium salt for white rats is 21.8 mg.; the M. T. D. 16.4 mg.; the M. E. D. for Trypanosoma equiperdum infections in the above animals 1.64 mg.,[1527] and the minimum therapeutic dose 2.4 mg. per kg.[1526] According to Hata [1533] the tolerated dose for mice by subcutaneous injection is 16.5 mg., for rats by intravenous administration 35 mg., while the dose tolerated by rabbits intravenously is 15 mg. per kg. In chickens infected with spirillæ the tolerated dose is 30 mg. and the curative dose 1.5 mg. per kg.[1534]

4-Arsenophenylglycine in the form of its disodium salt is tolerated intravenously by white rats in maximum doses of 118 mg. per kg., the M. L. D. being 197 mg. and the M. E. D. in Trypanosoma equiperdum infection 11.8 mg. per kg.[1527] The tolerated dose for hens is 400 mg. intramuscularly, but immediate sterilization is obtained in chicken spirillosis with doses of 100 to 200 mg. per kg., while with smaller doses sterilization occurs less rapidly.[1535] In rabbit syphilis the above compound acts more slowly than arsphenamine. With doses of 50 to 100 mg. per kg. intravenously the spirochetes do not disappear for several days; with a dose of 150 mg., however, they disappear immediately.[1536]

4,4′-Bismethylamino-3,5,3′,5′-tetraaminoarsenobenzene is claimed to be very efficient in the treatment of experimental syphilis and recurrent fever.[1537] In the latter infection, according to Mühlens, it is at least as effective as neoarsphenamine, and, in addition, can be more satisfactorily employed in the tropics as its solution is very stable in sealed tubes. The compound also yields good results in the treatment of malaria.[1538]

4,4′-Dihydroxyarsenobenzene produces permanent cures in mice infected with Spirocheta recurrentis by employing two subcutaneous injections of the drug in doses of 25 mg. per kg. Its tetrachloro and tetrabromo derivatives are somewhat less effective with the same infection, permanent cures being obtained only occasionally even when the infection is weaker, and repeated injections of the maximum tolerated doses are employed.[1539]

Arsphenamine.—This drug is recognized as the remedy of paramount value in syphilis. Despite the fact that it does not kill spirillæ in the test tube it has a very pronounced effect upon them in vivo due to its high parasitotropic influence and low organotropic effect. It is not only about fifty times less toxic for experimental animals than mercury,

but also has a roborant or tonic effect, which mercury does not possess.

Among the first experiments performed by Ehrlich after the elaboration of "salvarsan" (arsphenamine) was the determination of its toxic and therapeutic doses in mice, rats, hens and rabbits, when treated intravenously, intramuscularly and subcutaneously. He also noted that by injecting a sufficient quantity of the drug into an animal some time before infection, the latter can be repressed, the drug acting as a therapeutic and immunizing agent.[1509] Since the days of Ehrlich the method of producing arsphenamine has been continually improved so that the results of toxicity and therapeutic power as obtained to-day are much more favorable. The following table shows the most modern results obtained with various animals: [1540]

Animal	*Route of injection*	*Average tolerated dose mg. per kg.*
Mouse	Subcutaneous	143
	Intravenous	143
Rat	Subcutaneous	342
	Intravenous	105
Hen	Intravenous	80
	Intramuscular	250
Pigeon	Intravenous	80
	Intramuscular	90
Rabbit	Subcutaneous	150
	Intravenous	100

The slow injection of therapeutic quantities of arsphenamine in very dilute alkaline solution produces no striking results in anesthetized dogs. Upon increasing the rate of injection and the concentration of the drug, however, toxic symptoms soon begin to manifest themselves. The earliest of these consist of a dilation of the heart, a progressively increasing pulmonary blood-pressure and a slow, gradual, but not severe, fall of the systemic pressure.[1541] The rise in pulmonary pressure is largely due to a mechanical blocking or to a constricting action of the pulmonary vessels, depending upon the amount of alkali used in making the solution. The cardiac dilation does not appear to be a direct effect of the action of the drug, but rather secondary to the pulmonary obstruction, causing the right heart to work under undue strain and, secondarily, to dilate.[1542]

The average therapeutic dose of American-made arsphenamine administered intravenously into rats infected 24 hours previously with Trypanosoma equiperdum has been found to be 2 mg. per kg. by the method of Kolmer, Schamberg and Raiziss.[1516, 1526] Raiziss and Severac,[1543] employing white rats infected with 150,000 to 250,000 trypanosomes per cubic millimeter of blood, obtained temporary sterilization with doses of 6 mg., and permanent sterilization with those of 8 to 12 mg. per kg. by

the method of Voegtlin. The results obtained for other microparasites may be found in the following table: [1544]

Animal	Infection	Route of administration	Sterilizing dose mg. per kg.
Mouse	Recurrent fever	Subcutaneous	106.6
	Recurrent fever	Intravenous	106.6
Hen	Spirillosis	Intramuscular	3.5
Rabbit	Syphilis	Intravenous	23.5

Among the first observations made by various syphilologists in the treatment of human syphilis with arsphenamine was the occurrence of untoward symptoms or "reactions" which were at times very severe and in some cases even ended fatally. These symptoms may be classified under three heads: (1) those occurring immediately, e.g., flushing of the face, lachrymation, edema, swelling of the lips, tongue and eyelids, nausea, vomiting and retching, unconsciousness and, in rare instances, death; (2) those appearing within 24 hours, e.g., chilliness, rigor, headache, vertigo, diarrhœa and rise of temperature; (3) those observed after 24 hours, e.g., epileptiform convulsions, dilation of the pupils, absent reflexes, coma and even death. In addition there have been observed various mild skin eruptions, also cases of exfoliative dermatitis, jaundice and serous apoplexy or hemorrhagic encephalitis. The causes of the varied "reactions" following the administration of arsphenamine have never been definitely determined. They are dependent upon factors related to (1) the patient, e.g., individual susceptibility, physical condition; (2) the technic of administration, e.g., the purity, temperature and volume of water employed in dissolving the drug, the rate of injection, the alkalinity of the solution; and (3) the medicament itself, e.g., the nature and quantity of impurities.[1545] The majority of investigators regard the latter as the probable cause of disturbances in the patient, despite the fact that the analytical study of arsphenamine shows that the amount of impurity present in the drug must be very small.[121] According to Danysz [1546] the "reactions" are not due to the toxicity of the drug but to emboli caused by the intravascular precipitation of the compound by an excess of certain inorganic ingredients of the blood. There is no adequate evidence, however, that precipitation occurs after the use of a solution of the disodium salt of arsphenamine.[1547]

The introduction of arsphenamine into therapy about 14 years ago marked a new era in the treatment of syphilis. Its use has been attended by remarkable results upon syphilitic lesions in particular, and upon the course of the disease in general. When injected intravenously, the drug produces practically immediate relief to the patient and in many cases causes the disappearance of spirochetes from lesions within 24 hours. These results are not only due to the great destructive effect of arsphenamine upon the spirochetes of human syphilis but also to the

low toxicity of the drug, which permits of the administration of large doses. Such remarkable effects cannot be attained with mercury, even in massive doses. Raiziss and Severac have observed the complete disappearance of trypanosomes from the blood of heavily infected rats as early as three hours after the intravenous administration of arsphenamine or neoarsphenamine, so that these drugs may well be regarded as medicaments of inestimable value in the treatment and control of human syphilis.

Sodium silver arsphenamine, according to Knopf and Sinn,[1548] is not more effective than arsphenamine in the treatment of human syphilis, while Dreyfus[1549] claims that it is not only less convenient to handle than neoarsphenamine but more frequently produces "reactions" in patients. On the other hand, Koile[1550] found that it is superior to arsphenamine in both human and experimental syphilis; that the chemotherapeutic index in rabbit syphilis is 25 to 30, and that it produces sterilization within a comparatively short time. Fabry[1551] also obtained rapid cures in syphilis, but observed that it was not free of "reactions." Lenzmann[1552] found that although the results obtained with the drug in adults are very satisfactory, it is not readily tolerated by children. Another disadvantage is the greater care required in the technic of administration.

The introduction of methyl groups into the amino radicals increases the toxicity of arsphenamine. Thus, 3,3′-dimethyldiamino- and 3,3′-tetramethyldiamino-4,4′-dihydroxyarsenobenzenes are about 10 times as toxic as the parent substance, while 3,3′-hexamethyldiammonium-4,4′-dihydroxyarsenobenzene is 3 to 5 times as toxic. In addition, the hexa- and tetramethyl derivatives were without effect upon animals infected with trypanosomes, while the dimethyl compound sterilized the animal for a few days, after which a relapse occurred causing death.[642]

The introduction of carboxyl groups into the benzene rings of arsphenamine has a distherapeutic effect;[1553] iodine behaves similarly. Thus, 5,5′-diiodo-3,3′-diamino-4,4′-dihydroxyarsenobenzene produces a permanent cure in mice infected with Spirocheta recurrentis in doses of 41.5 mg. per kg., but as the maximum tolerated dose is 50 mg. per kg., its chemotherapeutic index is much less than that of arsphenamine.[649]

It has also been found that the introduction of amino groups into arsphenamine has an unfavorable influence upon the toxicity. Thus, 3,5,3′,5′-tetraamino-4,4′-dihydroxyarsenobenzene is 39 per cent more toxic than arsphenamine, while its therapeutic effect is the same as that of the parent substance.[1554]

Neoarsphenamine, when injected intravenously into rats, is about two and one-half times less toxic than the arsphenamine from which it is made, the average maximum tolerated dose of the American product

being 254 mg. per kg.[1540] With other test animals the following figures have been obtained: [1544]

Animal	*Route of administration*	*Average M. T. D. mg. per kg.*
Mouse	Intravenous	250
	Subcutaneous	85
Hen	Intravenous	60
	Intramuscular	10
Pigeon	Intravenous	120
	Intramuscular	40
Rabbit	Intravenous	200
	Subcutaneous	100

On the other hand, the average minimum curative dose of neoarsphenamine administered intravenously, according to the technic of Schamberg, Kolmer and Raiziss,[1592] into rats infected with Trypanosoma equiperdum, is 3 to 4 mg. per kg.[1526] Similar results were obtained by Raiziss and Severac, who, employing the same technic as well as that of Voegtlin, found the dose to be 4 to 6 mg. per kg.[1543] The values obtained with other animals are expressed in the following table: [1544]

Animal	*Infection*	*Route of administration*	*Sterilizing dose mg. per kg.*
Mouse	Recurrent fever	Subcutaneous	166.5
	Recurrent fever	Intravenous	199.8
Hen	Spirillosis	Intramuscular	6
Rabbit	Syphilis	Intravenous	30-40

Neoarsphenamine is, as a rule, better tolerated by patients than arsphenamine, but, like the latter, it also produces "reactions," the causes of which are as yet unknown. Unlike arsphenamine it has no effect on the pulmonary pressure when injected intravenously into dogs. Furthermore, it is not hemolytic, except in very dilute solutions (0.9 g. in 180 c.c. of water) or in extremely concentrated solutions (0.9 g. in 2 to 3 c.c.) while arsphenamine is hemolytic in practically all concentrations in which it is used. Another fact of importance is the hydrogen-ion concentration of these two compounds—in the case of neoarsphenamine it is 7 to 7.4, which is approximately the same as that of the blood, whereas a properly alkalinized solution of arsphenamine has a hydrogen-ion concentration beyond 9. Therefore, there is less biochemical disturbance of the blood and tissues after the administration of neoarsphenamine.

Despite the fact that some syphilologists still regard arsphenamine superior to neoarsphenamine, the latter is nevertheless more widely employed, as it exerts practically the same favorable influence upon the

disease with a greater degree of safety. The dictum enunciated many years ago, "Once a syphilitic, always a syphilitic," is gradually giving way to the belief that syphilis is curable with the aid of such powerful remedies as arsphenamine and neoarsphenamine. The economic and social benefits to the community effected by the use of arsphenamine and neoarsphenamine have been enormous. One of the most important results of the use of these powerful remedies is that the patient soon after treatment is rendered relatively innocuous as far as transmitting the disease to others is concerned. We can gain some idea of the extent of the use of arsphenamine and neoarsphenamine in therapy when we consider that about two million doses of American-made products are employed annually in the United States, about one-half of which is dispensed to indigent patients by the various state boards of health. During the war our Army and Navy alone utilized hundreds of thousands of doses of these arsenicals manufactured in this country, and the results obtained were so striking that patients were again rendered fit for military service within a very short time.[1555]

Silver neoarsphenamine.—The chemotherapeutic index of this compound in rabbit syphilis almost equals that of silver arsphenamine. The absolute quantity of the compound required to effect the complete disappearance of chancres is slightly larger than that of silver arsphenamine, but smaller than that required in the case of neoarsphenamine. Furthermore, silver neoarsphenamine is only about one-half as toxic as silver arsphenamine, and slightly more toxic than neoarsphenamine, as seen in the following values obtained by Kolle: [1593]

		Maximum Tolerated Dose per kg.
Mice	Silver neoarsphenamine	278 mg.
	Neoarsphenamine	370 "
	Silver arsphenamine	167 "
Rabbits	Silver neoarsphenamine	160 mg.
	Neoarsphenamine	220 "
	Silver arsphenamine	110 "

The most significant feature connected with its clinical application is its failure to produce the angioneurotic symptom complex. It combines the chemotherapeutic superiority of silver arsphenamine with the important practical advantages of neoarsphenamine, such as ease of solubility and comparatively low toxicity. In addition, its aqueous solution is practically stable in air.

Sulpharsphenamine is tolerated intravenously by white rats in doses of 300-400 mg. per kg., while the minimum curative dose in the same species infected with Trypanosoma equiperdum is two to three times

that of neoarsphenamine.[1543] According to Voegtlin[718] the M. L. D. for white rats ranges from 320 to 480 mg., and the M. E. D. from 15.9 to 31.5 m. per kg. when administered intravenously. When injected subcutaneously in the same species, the M. L. D. is 400 to 700 mg. and the M. E. D. 15.6 to 34 mg. per kg. In rabbits injected intravenously the M. L. D. is 320 mg. per kg. From these figures it can be seen that sulpharsphenamine is much less toxic than arsphenamine and compares favorably in this respect with neoarsphenamine.

According to Voegtlin the trypanocidal power of sulpharsphenamine approximately equals that of the average sample of commercial neoarsphenamine, but the results obtained by Raiziss show that it is inferior to the latter in this respect. In addition, it acts more slowly upon Trypanosoma equiperdum than either arsphenamine or neoarsphenamine. Sulpharsphenamine is best adapted for subcutaneous or intramuscular medication—the latter being generally preferred, especially in the treatment of children or when the veins are small or inaccessible.

3,3′-Diacetyldiamino-4,4′-dihydroxyarsenobenzene acts more favorably than arsphenamine when injected subcutaneously into mice, the M. T. D. being 500 mg. and the minimum curative dose, 83.5 mg. per kg. In rabbit syphilis or chicken spirillosis, however, its curative power is less than that of arsphenamine.[649]

3,3′-Dicarbamido-4,4′-dihydroxyarsenobenzene cures mice infected with Spirocheta recurrentis in doses of 166.5 mg. per kg., while the M. T. D. is 500 mg. per kg.[649]

The **arsenostibino compounds** exhibit an appreciable curative power in animals infected with trypanosomes. This is especially true of 3-amino-4-hydroxyarseno-4′-acetylaminostibinobenzene hydrochloride.[1556]

Phenylarsonic and **4-methylphenylarsonic acids** are both effective trypanocides, but they are also very toxic.[1557]

4-Iodo-, Iodoso- and **Iodoxyphenylarsonic acids** have approximately the same toxicity, which amounts to 25 mg. per kg. It is interesting to note that the iodo and iodoso derivatives produce icterus in mice, while the iodoxy compound does not.[904]

p-Arsanilic acid and **atoxyl.**—As early as 1902 Blumenthal[1558] showed that atoxyl produces favorable results in cases of chlorosis, anemia and carcinoma, while Schildt[1559] obtained cures in xanthoma diabeticorum and lichen ruber, and also improvements in cases of psoriasis by employing atoxyl subcutaneously. Three years later Thomas and Breinl[1560] found that the same compound effected cures in experimental trypanosomiasis in mice. In 1907 Koch reported beneficial

results in the treatment of sleeping sickness by means of atoxyl.[1561] This was followed by a series of extensive investigations by many scientists, among whom were Ehrlich, Hata, Shiga, Levaditi, MacIntosh, Uhlenhuth, Gross, Manteufel,[1562] Mulzer,[1563] Bitter, Dreyer,[1509] Nierenstein,[1564] Bickel,[1565] Hoffman, Roscher,[1566] Salmon,[1567] Hallopeau,[1568] Metschnikoff, Neisser, Lesser and Iversen.[1569] Thus, it was shown by Ehrlich and Shiga that atoxyl is without effect upon trypanosomes in vitro but is active in vivo. More or less favorable results were obtained by the above investigators in experimental trypanosomiasis, chicken spirillosis and even in human syphilis. Later Schamberg, Kolmer and Raiziss demonstrated that complete cures may be obtained in white rats infected with Trypanosoma equiperdum. It soon became evident, however, that the compound is very dangerous for human medication, as it produces nervous disorders and affects the optic nerve, causing either temporary or permanent blindness. Although the greater part of the atoxyl introduced into the body appears in the urine unchanged, its toxic action is probably due to a splitting off of arsenic, which produces the usual symptoms of arsenic poisoning, and to the reduction of a part of the atoxyl by various body cells, the resulting compound inducing local poisoning.[1569]

Within recent years Raiziss has found that pure arsanilic acid is tolerated by white rats in doses as high as 150 mg. per kg. when introduced intravenously, while according to Voegtlin and Smith[1527] the M. T. D. of anhydrous atoxyl is 239 mg., the M. L. D. 358.5 mg. and the M. E. D. in experimental trypanosomiasis is 89.6 mg. per kg.

Uhlenhuth and his associates investigated a mercurated derivative of atoxyl with which they obtained better results in rabbit, chicken and human syphilis than with atoxyl itself.

Sodium acetyl-p-arsanilate (Arsacetin) is tolerated, according to Ehrlich, in doses from 3 to 10 times as large as that of atoxyl, depending upon the individual experimental animal.[1570] Breinl found it effective in curing experimental trypanosomiasis, while in experimental recurrent fever Hata observed that it does not produce prolonged sterilization, although it yields better results than atoxyl. In cases of relapsing fever, patients treated successively with atoxyl and arsacetin become resistant toward the latter, thereby confirming Ehrlich's theory regarding drug-fastness in trypanosome or spirochetal infections.[1509] According to the most recent investigations the M. L. D. of arsacetin is 2.108 g., the M. T. D., 1.405 g., and the M. E. D., 105.4 mg. per kg.[1527] It is tolerated by healthy hens in doses of 125 mg. per kg., while the curative dose in chicken spirillosis is 30 to 40 mg. per kg.[1571]

4-Sulfomethylaminophenylarsonic acid.—The introduction of a sulfomethyl- group into the amino radical of p-arsanilic acid reduces

not only the toxicity, but also the curative power of the parent compound.[1043]

Tryparsamide (N-phenylglycineamide-4-arsonic acid).—This compound yields satisfactory results by the various methods of administration and can be given in very large doses. The following table shows the M. L. D. for various experimental animals arranged according to the method of injection:

Animal	*Intravenous g. per kg.*	*Intraperitoneal g. per kg.*	*Subcutaneous g. per kg.*
Mouse	2.0	2.0–2.25	2.5–2.75
Rat	...	0.75–1.75	1.0
Guinea pig	...	1.5	1.5
Rabbit	0.75–0.9	1.1	...
Monkey	1.25–1.5	...	...

The toxic effects of the drug are confined to doses relatively close to the M. L. D., and the recovery of animals from sublethal intoxications is remarkably rapid and complete. This makes possible the repeated administration of even very large doses of the drug at comparatively short intervals, without incurring the dangers incident to cumulative action or to superposition of toxic effects. On the contrary, by taking advantage of this peculiarity of action, it is possible to develop such a degree of tolerance on the part of animals that the dose of the drug administered can be progressively increased to a point well above that which is fatal to the normal animal. This stands out as the feature of its toxicologic action, which is of greatest significance in the use of the drug for therapeutic purposes.

The minimum curative dose with mice infected with Trypanosoma brucei is 275 mg. per kg. intraperitoneally, and 200 mg. intravenously. With Trypanosoma equiperdum in the same species the minimum curative dose is 225 mg. per kg. intraperitoneally; for rats the dose required ranges from 250 to 500 mg. per kg. intraperitoneally, while in the case of guinea pigs cures are obtained with 150 to 250 mg. per kg. The rapidity of the trypanocidal action of the drug in the above animals is quite marked, i.e., with curative doses, the drug becomes quickly available after its administration, and remains in an active biological state long enough to accomplish its trypanocidal action, for in 18 to 24 hours after the treatment of a 24-hour infection, the peripheral blood is free of parasites. Its chemotherapeutic index for mice in the preceding experiments is 8, for rats 3 and for guinea pigs 10.

Tryparsamide also exhibits a marked trypanocidal activity in human trypanosomiasis caused by Trypanosoma gambiense, single doses of 0.5 to 5.0 g. producing peripheral sterilization of the blood and lymph glands in from 6 to 12 hours. The immediate trypanocidal action after intramuscular administration is as rapid as that following the intravenous

route, while the duration of peripheral sterilization is appreciably longer. The general beneficial effect of the drug is a noticeable feature of its action in both early and advanced cases as shown by the disappearance of subjective symptoms, by the return of the pulse and temperature to normal limits, by the pronounced improvement of the blood picture and by well-marked gains in weight.[1572]

3,5-Dichloro-4-hydroxyphenylarsonic acid is tolerated by mice in doses of 666.5 mg. per kg., and sterilizes the same animals infected with Spirocheta recurrentis in doses of 500 mg. per kg. Unfortunately, this compound subsequently produces disturbances in the nervous system of the experimental animals, and for this reason has never found practical application in therapy.[1573]

3-Amino-4-hydroxyphenylarsonic acid can be tolerated by white rats in doses as high as 500 mg. per kg., while the minimum sterilizing dose for the same species infected with Trypanosoma equiperdum is 80 mg. per kg., both tests being carried out intravenously.[582] According to Hata[1574] it is tolerated by mice in doses as high as 1250 mg., while the sterilizing dose for recurrent fever in the same animal is 833.5 mg. per kg. However, it is claimed that it cannot be employed in practical therapy, as it seriously affects the nervous system. The results obtained in white rats by Voegtlin and Smith with the sodium salt of this acid are: M. L. D., 637.5 mg., M. T. D., 382.5 mg., while the M. E. D., employing Trypanosoma equiperdum, is 95.6 mg. per kg.[1527]

Mercurated arsonic acids are not superior to the corresponding non-arsenated mercurials with regard to germicidal or curative value.[1541]

Elarson (strontium chloroarsinosobehenolate) is ineffective in mice infected with trypanosomes. When injected intravenously, it not only lowers the blood pressure but is also more toxic than arsenious acid.[1575]

Appendix II. Analyses of Organic Arsenicals.

The following methods have been employed by various investigators for the estimation of arsenic:

1. The method of Carius.

2. A mixture of the arsenical and soda-lime is heated in a current of oxygen, the resulting mass dissolved in hydrochloric acid, and the arsenic precipitated as the trisulfide by hydrogen sulfide. The precipitate is then dissolved in fuming nitric acid and finally weighed as magnesium pyroarsenate.[1576]

3. The substance is decomposed in a porcelain crucible with a solution of magnesium oxide in nitric acid (d, 1.38) by heating first on a water-bath, then in a sand-bath, and finally over a free flame. The residue is taken up with hydrochloric acid, and the arsenic finally precipitated with magnesia mixture.[1577]

4. The compound is destroyed by warming with chromic and sulfuric acids. The arsenic is precipitated as the trisulfide, which is then oxidized with ammoniacal hydrogen peroxide, precipitated as magnesium ammonium arsenate, and finally weighed as the pyroarsenate.[1578]

5. The substance is decomposed by heating with pure zinc oxide. The mass is then dissolved in acid, the arsenic precipitated as the trisulfide which is then oxidized to arsenic acid and finally weighed as magnesium pyroarsenate.[1579]

6. The organic arsenical is fused with sodium peroxide in a silver crucible, the resulting mass dissolved in water, evaporated twice with nitric acid, and the arsenic weighed as magnesium pyroarsenate.[1580]

7. 0.2 to 0.3 g. of the finely powdered substance is fused with 10-15 g. of a mixture of equal parts of sodium peroxide and sodium carbonate, the mass extracted with water and rinsed into a 450 c.c. conical flask. From 25 to 31 c.c. of sulfuric acid (1:1) are cautiously added, and, if necessary, the solution is boiled down to 100 c.c. 1 g. of potassium iodide is now introduced, and the liquid further concentrated to 40 c.c. A few drops of dilute sulfurous acid are added to destroy the last traces of iodine, and the bright green solution is diluted with hot water and saturated with hydrogen sulfide. The arsenic trisulfide is washed about three times with hot water, dissolved off the filter with 20 c.c. of 0.1 N-sodium hydroxide and treated with 30 c.c. of hydrogen peroxide, the excess being destroyed by heating on the water-bath for 10 minutes. After the frothing has subsided, a few drops of phenolphthalein are added, followed by 11 c.c. of sulfuric acid (1:1). Potassium iodide

(1 g.) is now added to the liquid, which is then concentrated to 40 c.c. and the pale yellow color removed by a few drops of dilute sulfurous acid. After adding a volume of 10 per cent sodium phosphate solution equal to the number of cubic centimeters of 0.1 N-iodine required in the titration, the arsenite solution is titrated with standard iodine in the usual way.

A variation of this method consists in oxidizing the precipitate of arsenic trisulfide with alkaline hydrogen peroxide, and precipitating as magnesium ammonium arsenate.[1581]

8. 0.2 to 0.4 g. of the finely powdered compound is fused with a mixture of 10 g. of finely powdered, dry potassium nitrate and 5 g. of sodium peroxide in a nickel crucible. The melt is then dissolved in hot water, and the solution carefully acidified with hydrochloric acid. After filtering, the liquid is neutralized with ammonia, the arsenic precipitated as magnesium ammonium arsenate and weighed as magnesium pyroarsenate.[1582]

9. 0.25 to 0.3 g. of the compound is decomposed by the Kjeldahl method, using 25 c.c. of concentrated sulfuric acid, 10 g. of potassium sulfate and a very small crystal of copper sulfate. After the destruction of the organic matter and dilution with water, the arsenic is precipitated by hydrogen sulfide, and determined gravimetrically in the usual way as magnesium pyroarsenate.[911]

10. Lehmann's method:[1583] The substance (0.2 g.) is transferred to a 200 c.c. ground glass stoppered Erlenmeyer flask, and 1 g. of finely powdered potassium permanganate added, followed by 5 c.c. of dilute sulfuric acid. The mixture is allowed to stand for 5-10 minutes, during which time the flask is frequently rotated to insure the complete mixing of the materials. 10 c.c. of concentrated sulfuric acid are now added in portions of about 2 c.c., the flask being rotated after each addition. When the reaction has ceased, 3 per cent hydrogen peroxide (5-10 c.c.) is added in small portions until all the manganese dioxide has been dissolved. Toward the end the hydrogen peroxide should be added drop by drop to avoid a large excess. The liquid is then diluted with 25 c.c. of distilled water and boiled for about 10 minutes until the excess of peroxide has been completely destroyed. The remaining solution is then diluted with 50 c.c. of distilled water, cooled and 2.5 g. of potassium iodide added. The flask is now tightly stoppered, allowed to stand for one hour in a dark place, and the liberated iodine titrated with standard sodium thiosulfate without a starch indicator.

Myers and DuMez[1584] have found it practically impossible to remove all of the excess of hydrogen peroxide by boiling, unless the solution is evaporated to a very small volume, when it is liable to become colored brown, due to the further action of the hot concentrated sulfuric acid. Accordingly, they removed the last trace of hydrogen peroxide by adding a drop or two of permanganate solution (1 per cent)

and destroying the resulting pink color by the addition of a very slight excess of oxalic acid solution. The same investigators also suggested that a blank test be carried out under exactly the same conditions and the final reading corrected accordingly. Fargher's modification[1585] is the same as that of Myers and DuMez except that before the addition of the hydrogen peroxide the mixture is heated to gentle boiling for 30 minutes with 10 c.c. of water.

The modified method is simple, accurate, reliable, inexpensive and rapid. It cannot be used with all organic arsenicals, however, as certain compounds, e.g., benzarsonic acid, are not completely oxidized by the preliminary treatment with potassium permanganate and sulfuric acid.

11. The following method is quoted from the *Pharmacopœia Germanica:*[1586]

The arsenic compound (0.2 g.) is oxidized by means of 10 c.c. of concentrated sulfuric acid and 1 c.c. of fuming nitric acid in a long-necked 100 c.c. Jena flask. After boiling for one hour, the cooled mixture is treated with 50 c.c. of water, evaporated, and the procedure repeated. To the cold solution are now added successively 10 c.c. of water, 2 g. of potassium iodide in 5 c.c. of water, and sufficient water to dissolve the precipitate. After standing for thirty minutes, the liberated iodine is titrated without an indicator.

12. Another procedure consists in transferring the sample (0.5 g.) into a 500 c.c. Erlenmeyer flask, adding about 10 c.c. of water, then 5 c.c. of nitric acid, heating on a hot plate, and adding ammonium persulfate until the solution is water-white. If the decomposition is extremely difficult and a yellow color persists, boiling for a few minutes with a few cubic centimeters of water and several grams of ammonium persulfate will produce decolorization. The solution is then diluted up to 100 c.c. and treated with a saturated solution of sodium ammonium hydrogen phosphate (5 c.c.) followed by an excess of magnesia mixture (about 40 c.c.). If a precipitate forms it is redissolved in dilute nitric acid. The whole is then maintained at or near the boiling point, an excess of ammonia added, and the liquid allowed to stand for about two hours. The resulting precipitate is filtered off, washed with dilute ammonia, and dissolved in 70 c.c. of dilute hydrochloric acid (3:2). To the solution are added successively 3 g. of potassium iodide dissolved in 6 c.c. of water, and 70 c.c. of water, and the liberated iodine titrated with sodium thiosulfate, using starch on approaching the end point.[1587]

13. Ewins' method: The substance (0.1 to 0.2 g.) is mixed in a 300 c.c. Kjeldahl flask with 10 g. of potassium sulfate, 0.2 to 0.3 g. of starch and 20 c.c. of concentrated sulfuric acid. The whole is warmed gently over a Bunsen flame for 10 to 15 minutes until the frothing diminishes, and then vigorously for about four hours, when complete oxidation occurs. The liquid is cooled, transferred to a 350 c.c. Erlenmeyer flask and rendered barely alkaline to litmus by means of 10-12

N-sodium hydroxide. The flask and its contents are then cooled to about 30-40°, concentrated sulfuric acid added drop by drop until the solution is again distinctly acid, and a saturated solution of sodium bicarbonate added until the whole is distinctly alkaline and an excess of 5 to 10 c.c. of the reagent is present. The arsenious acid is then titrated with 0.05 N-iodine solution, employing 2 c.c. of a 1 per cent starch solution as an indicator. Toward the end of the titration, the solution usually develops a reddish-violet tint which fades on standing. The end point, however, is reached when the solution acquires the characteristic permanent deep blue color given by free iodine in the presence of starch.[1588]

14. By another method 0.2 g. of the substance is weighed into a 150 c.c. Erlenmeyer flask, and heated with 5.5 c.c. of concentrated sulfuric acid and 1 c.c. of fuming nitric acid for about one hour. The flask is then slightly cooled, 10 or 15 drops of fuming nitric acid added, and the whole heated for 5 minutes to insure complete oxidation. After cautiously adding 1 g. of solid ammonium sulfate, the flask is first shaken until the evolution of nitrogen is complete, then cooled, and the liquid diluted with water to 60 or 70 c.c. To the mixture are added 1 g. of potassium iodide and a few grains of porous clay plate, and a simple bulb trap, such as an inverted 25 c.c. flask with a side vent, is placed in the mouth of the Erlenmeyer flask. The liquid is now concentrated to a volume of 40 c.c. and the bulb trap rinsed into the flask. After removing the iodine tint by means of 0.01 N-thiosulfate, the solution is diluted to 100-120 c.c. with cold water, transferred to a 500 c.c. Erlenmeyer flask containing 50 c.c. of 4 N-sodium carbonate solution, and the residual acid neutralized with a slight excess of sodium bicarbonate. Starch solution is then added and the arsenite present titrated with standard iodine solution. No blank is necessary.[1589]

Carbon and hydrogen in organic arsenicals are determined:

1. By combustion with a mixture of lead chromate and copper oxide in a current of oxygen.[1579]

2. By a modification of the Dennstedt procedure described by Falkov and Raiziss.[1590] Both the apparatus and the procedure are identical with those described by Dennstedt [1591] except that the wider part of the

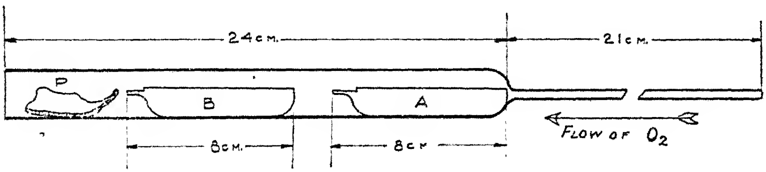


FIG. 3.—INNER TUBES FOR ANALYSIS OF ORGANIC ARSENICALS.

A, porcelain boat with substance; B, porcelain boat with red lead; P, a piece of broken porcelain to prevent the accidental deposition of any particles upon the catalyst.

inner tube is 5 or 6 cm. longer, and that Boat B containing red lead is placed 3 cm. from Boat A (Fig. 3).

The red lead reacts quantitatively with the arsenic oxide formed during the combustion, forming lead arsenate which does not decompose at comparatively high temperatures. This stability of the lead arsenate is of great convenience as carbonaceous matter, which frequently settles upon it, can be entirely removed by continued heating. The red lead is prepared from pure lead peroxide, by drying in an oven at 140° and then gradually heating it in a current of oxygen until it is dark red, after which it is cooled and kept in a desiccator.

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